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ADDITIONAL HETEROPOLYCYCLIC COMPOUNDS AND THEIR USE AS METABOTROPIC GLUTAMATE RECEPTOR ANTAGONISTS

FIELD OF THE INVENTION

[0001] The present invention relates to a new class of compounds, to pharmaceutical formulations containing said compounds and to the use of said compounds in therapy. The present invention further relates to the process for the preparation of said compounds and to new intermediates prepared therein.

BACKGROUND OF THE INVENTION

[0002] Glutamate is the major excitatory neurotransmitter in the mammalian central nervous system (CNS). Glutamate produces its effects on central neurons by binding to and thereby activating cell surface receptors. These receptors have been divided into two major classes, the ionotropic and metabotropic glutamate receptors, based on the structural features of the receptor proteins, the means by which the receptors transduce signals into the cell, and pharmacological profiles.

[0003] The metabotropic glutamate receptors (mGluRs) are G protein-coupled receptors that activate a variety of intracellular second messenger systems following the binding of glutamate. Activation of mGluRs in intact mammalian neurons elicits one or more of the following responses: activation of phospholipase C; increases in phosphoinositide (PI) hydrolysis; intracellular calcium release; activation of phospholipase D; activation or inhibition of adenyl cyclase; increases or decreases in the formation of cyclic adenosine monophosphate (cAMP); activation of guanylyl cyclase; increases in the formation of cyclic guanosine monophosphate (cGMP); activation of phospholipase A_2; increases in arachidonic acid release; and increases or decreases in the activity of voltage- and ligand-gated ion channels. Schoepp *et al.*, *Trends Pharmacol. Sci. 14*:13 (1993), Schoepp, *Neurochem. Int. 24*:439 (1994), Pin *et al.*, *Neuropharmacology 34*:1 (1995), Bordi and Ugolini, *Prog. Neurobiol. 59*:55

[0004] Molecular cloning has identified eight distinct mGluR subtypes, termed mGluR1 through mGluR8. Nakanishi, *Neuron 13*:1031 (1994), Pin *et al.*, *Neuropharmacology 34*:1 (1995), Knopfel *et al.*, *J. Med. Chem. 38*:1417 (1995). Further receptor diversity occurs via expression of alternatively spliced forms of certain mGluR subtypes. Pin *et al.*, *PNAS 89*:10331 (1992), Minakami *et al.*, *BBRC 199*:1136 (1994), Joly *et al.*, *J. Neurosci. 15*:3970 (1995).

[0005] Metabotropic glutamate receptor subtypes may be subdivided into three groups, Group I, Group II, and Group III mGluRs, based on amino acid sequence homology, the second messenger systems utilized by the receptors, and by their pharmacological characteristics. Group I mGluR comprises mGluR1, mGluR5 and their alternatively spliced variants. The binding of agonists to these receptors results in the activation of phospholipase C and the subsequent mobilization of intracellular calcium.

Neurological, psychiatric and pain disorders

[0006] Attempts at elucidating the physiological roles of Group I mGluRs suggest that activation of these receptors elicits neuronal excitation. Various studies have demonstrated that Group I mGluRs agonists can produce postsynaptic excitation upon application to neurons in the hippocampus, cerebral cortex, cerebellum, and thalamus, as well as other CNS regions. Evidence indicates that this excitation is due to direct activation of postsynaptic mGluRs, but it also has been suggested that activation of presynaptic mGluRs occurs, resulting in increased neurotransmitter release. Baskys, *Trends Pharmacol. Sci. 15*:92 (1992), Schoepp, *Neurochem. Int. 24*:439 (1994), Pin *et al.*, *Neuropharmacology 34*:1(1995), Watkins *et al.*, *Trends Pharmacol. Sci. 15*:33 (1994).

[0007] Metabotropic glutamate receptors have been implicated in a number of normal processes in the mammalian CNS. Activation of mGluRs has been shown to be required for induction of hippocampal long-term potentiation and cerebellar long-term depression. Bashir *et al.*, *Nature 363*:347 (1993), Bortolotto *et al.*, *Nature 368*:740 (1994), Aiba *et al.*, *Cell 79*:365 (1994), Aiba *et al.*, *Cell 79*:377 (1994). A

role for mGluR activation in nociception and analgesia also has been demonstrated, Meller *et al.*, *Neuroreport 4*: 879 (1993), Bordi and Ugolini, *Brain Res. 871*:223 (1999). In addition, mGluR activation has been suggested to play a modulatory role in a variety of other normal processes including synaptic transmission, neuronal development, apoptotic neuronal death, synaptic plasticity, spatial learning, olfactory memory, central control of cardiac activity, waking, motor control and control of the vestibulo-ocular reflex. Nakanishi, *Neuron 13*: 1031 (1994), Pin *et al.*, *Neuropharmacology 34*:1, Knopfel *et al.*, *J. Med. Chem. 38*:1417 (1995).

[0008] Further, Group I metabotropic glutamate receptors and mGluR5 in particular, have been suggested to play roles in a variety of pathophysiological processes and disorders affecting the CNS. These include stroke, head trauma, anoxic and ischemic injuries, hypoglycemia, epilepsy, neurodegenerative disorders such as Alzheimer's disease and pain. Schoepp *et al.*, *Trends Pharmacol. Sci. 14*:13 (1993), Cunningham *et al.*, *Life Sci. 54*:135 (1994), Hollman *et al.*, *Ann. Rev. Neurosci. 17*:31 (1994), Pin *et al.*, *Neuropharmacology 34*:1 (1995), Knopfel *et al.*, *J. Med. Chem. 38*:1417 (1995), Spooren et al., *Trends Pharmacol. Sci. 22*:331 (2001), Gasparini et al. *Curr. Opin. Pharmacol. 2*:43 (2002), Neugebauer *Pain 98*:1 (2002). Much of the pathology in these conditions is thought to be due to excessive glutamate-induced excitation of CNS neurons. Because Group I mGluRs appear to increase glutamate-mediated neuronal excitation via postsynaptic mechanisms and enhanced presynaptic glutamate release, their activation probably contributes to the pathology. Accordingly, selective antagonists of Group I mGluR receptors could be therapeutically beneficial, specifically as neuroprotective agents, analgesics or anticonvulsants.

[0009] Recent advances in the elucidation of the neurophysiological roles of metabotropic glutamate receptors generally and Group I in particular, have established these receptors as promising drug targets in the therapy of acute and chronic neurological and psychiatric disorders and chronic and acute pain disorders. Because of their physiological and pathophysiological significance, there is a need for new potent mGluR agonists and antagonists that display a high selectivity for mGluR subtypes, particularly the Group I receptor subtype, most particularly the mGluR5 subtype.

Gastro intestinal disorders

[0010] The lower esophageal sphincter (LES) is prone to relaxing intermittently. As a consequence, fluid from the stomach can pass into the esophagus since the mechanical barrier is temporarily lost at such times, an event hereinafter referred to as "G.I. reflux".

[0011] Gastro-esophageal reflux disease (GERD) is the most prevalent upper gastrointestinal tract disease. Current pharmacotherapy aims at reducing gastric acid secretion, or at neutralizing acid in the esophagus. The major mechanism behind G.I. reflux has been considered to depend on a hypotonic lower esophageal sphincter. However, e.g. *Holloway & Dent (1990) Gastroenterol. Clin. N. Amer. 19, pp. 517-535,* has shown that most reflux episodes occur during transient lower esophageal sphincter relaxations (TLESRs), i.e. relaxations not triggered by swallows. It has also been shown that gastric acid secretion usually is normal in patients with GERD.

[0012] The novel compounds according to the present invention are assumed to be useful for the inhibition of transient lower esophageal sphincter relaxations (TLESRs) and thus for treatment of gastro-esophageal reflux disorder (GERD).

[0013] The wording "TLESR", transient lower esophageal sphincter relaxations, is herein defined in accordance with *Mittal, R.K., Holloway, R.H., Penagini, R., Blackshaw, L.A., Dent, J., 1995; Transient lower esophageal sphincter relaxation. Gastroenterology 109,*
pp. 601-610.

[0014] The wording "G.I. reflux" is herein defined as fluid from the stomach being able to pass into the esophagus, since the mechanical barrier is temporarily lost at such times.

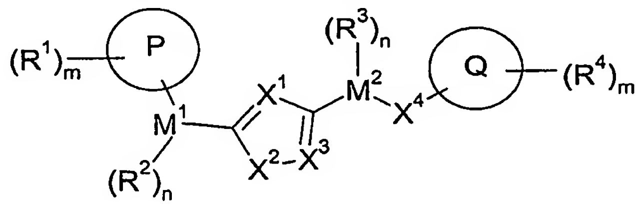
[0015] The wording "GERD", gastro-esophageal reflux disease, is herein defined in accordance with van Heerwarden, M.A., Smout A.J.P.M., 2000; Diagnosis of reflux disease. Baillière's Clin. Gastroenterol. 14, pp. 759-774.

[0016] Because of their physiological and pathophysiological significance, there is a need for new potent mGluR agonists and antagonists that display a high selectivity for mGluR subtypes, particularly the Group I receptor subtype.

[0017] The object of the present invention is to provide compounds exhibiting an activity at metabotropic glutamate receptors (mGluRs), especially at the mGluR5 receptor.

SUMMARY OF THE INVENTION

[0018] The present invention provides a compound of formula Ia



(Ia)

wherein:

[0019] P is selected from the group consisting of hydrogen, C_{3-7}alkyl or a 3- to 8-membered ring containing one or more atoms independently selected from C, N, O and S, which ring may optionally be fused with a 5- or 6-membered ring containing one or more atoms independently selected from the group consisting of C, N, O and S;

[0020] R^1 is selected from the group consisting of hydrogen, hydroxy, halo, nitro, C_{1-6}alkylhalo, OC_{1-6}alkylhalo, C_{1-6}alkyl, OC_{1-6}alkyl, C_{2-6}alkenyl, OC_{2-6}alkenyl, C_{2-6}alkynyl, OC_{2-6}alkynyl, C_{0-6}alkylC_{3-6}cycloalkyl, OC_{0-6}alkylC_{3-6}cycloalkyl, C_{0-6}alkylaryl, OC_{0-6}alkylaryl, CHO, $(CO)R^5$, $O(CO)R^5$, $O(CO)OR^5$, $O(CN)OR^5$, C_{1-6}alkylOR^5, OC_{2-6}alkylOR^5, C_{1-6}alkyl$(CO)R^5$, OC_{1-6}alkyl$(CO)R^5$, C_{0-6}alkylCO_2R^5, OC_{1-6}alkylCO_2R^5, C_{0-6}alkylcyano, OC_{2-6}alkylcyano, C_{0-6}alkylNR^5R^6, OC_{2-6}alkylNR^5R^6, C_{1-6}alkyl$(CO)NR^5R^6$, OC_{1-6}alkyl$(CO)NR^5R^6$, C_{0-6}alkyl$NR^5(CO)R^6$, OC_{2-6}alkyl$NR^5(CO)R^6$, C_{0-6}alkyl$NR^5(CO)NR^5R^6$, C_{0-6}alkylSR^5, OC_{2-6}alkylSR^5, C_{0-6}alkyl$(SO)R^5$, OC_{2-6}alkyl$(SO)R^5$, C_{0-6}alkylSO_2R^5, OC_{2-6}alkylSO_2R^5, C_{0-6}alkyl$(SO_2)NR^5R^6$, OC_{2-6}alkyl$(SO_2)NR^5R^6$,C_{0-6}alkyl$NR^5(SO_2)R^6$, OC_{2-6}alkyl$NR^5(SO_2)R^6$, C_{0-6}alkyl$NR^5(SO_2)NR^5R^6$, OC_{2-6}alkyl$NR^5(SO_2)NR^5R^6$, $(CO)NR^5R^6$, $O(CO)NR^5R^6$, NR^5OR^6, C_{0-6}alkyl$NR^5(CO)OR^6$, OC_{2-6}alkyl$NR^5(CO)OR^6$, SO_3R^5 and a 5- or 6-membered ring containing one or more

atoms independently selected from the group consisting of C, N, O and S, wherein said ring may be substituted by one or more A;

[0021] M^1 is selected from the group consisting of a bond, C_{1-3}alkyl, C_{2-3}alkenyl, C_{2-3}alkynyl, C_{0-4}alkyl(CO)C_{0-4}alkyl, C_{0-3}alkylOC_{0-3}alkyl, C_{0-3}alkyl(CO)NR^5, C_{0-3}alkyl(CO)NR^5C_{0-3}alkyl, C_{0-4}alkylNR^5, C_{0-3}alkylSC_{0-3}alkyl, C_{0-3}alkyl(SO)C_{0-3}alkyl or C_{0-3}alkyl(SO_2)C_{0-3}alkyl;

[0022] R^2 is selected from the group consisting of hydrogen, hydroxy, C_{0-6}alkylcyano, oxo, $=NR^5$, $=NOR^5$, C_{1-4}alkylhalo, halo, C_{1-4}alkyl, O(CO)C_{1-4}alkyl, C_{1-4}alkyl(SO)C_{0-4}alkyl, C_{1-4}alkyl(SO_2)C_{0-4}alkyl, (SO)C_{0-4}alkyl, (SO_2)C_{0-4}alkyl, OC_{1-4}alkyl, C_{1-4}alkylOR^5 and C_{0-4}alkylNR^5R^6;

[0023] X^1, X^2 and X^3 are independently selected from the group consisting of CR, CO, N, NR, O and S;

[0024] R is selected from the group consisting of hydrogen, C_{0-3}alkyl, halo, C_{0-3}alkylOR^5, C_{0-3}alkylNR^5R^6, C_{0-3}alkyl(CO)OR^5, C_{0-3}alkylNR^5R^6 and C_{0-3}alkylaryl;

[0025] M^2 is selected from a group consisting of a bond, C_{1-3}alkyl, C_{3-7}cycloalkyl, C_{2-3}alkenyl, C_{2-3}alkynyl, C_{0-4}alkyl(CO)C_{0-4}alkyl, C_{0-3}alkylOC_{0-3}alkyl, C_{0-3}alkylNR^5C_{1-3}alkyl, C_{0-3}alkyl(CO)NR^5, C_{0-4}alkylNR^5, C_{0-3}alkylSC_{0-3}alkyl, C_{0-3}alkyl(SO)C_{0-3}alkyl and C_{0-3}alkyl(SO_2)C_{0-3}alkyl;

[0026] R^3 is selected from a group consisting of hydrogen, hydroxy, C_{0-6}alkylcyano, oxo, $=NR^5$, $=NOR^5$, C_{1-4}alkylhalo, halo, C_{1-4}alkyl, O(CO)C_{1-4}alkyl, C_{1-4}alkyl(SO)C_{0-4}alkyl, C_{1-4}alkyl(SO_2)C_{0-4}alkyl, (SO)C_{0-4}alkyl, (SO_2)C_{0-4}alkyl, OC_{1-4}alkyl, C_{1-4}alkylOR^5 and C_{0-4}alkylNR^5R^6;

[0027] X^4 is selected from the group consisting of C_{0-4}alkylR^5, C_{0-4}alkyl(NR^5R^6), C_{0-4}alkyl(NR^5R^6)=N, NR^5C_{0-4}alkyl(NR^5R^6)=N, NOC_{0-4}alkyl, C_{1-4}alkylhalo, C, O, SO, SO_2 and S;

[0028] Q is a 5- or 6-membered ring containing one or more atoms independently selected from the group consisting of C, N, O and S, which group may optionally be fused with a 5- or 6-membered ring containing one or more atoms independently selected from the group consisting of C, N, O and S and which fused ring may be substituted by one or more A;

[0029] R^4 is selected from the group consisting of hydrogen, hydroxy, C_{0-}

$_{6}$alkylcyano, oxo, $=NR^5$, $=NOR^5$, C_{1-4}alkylhalo, halo, C_{1-4}alkyl, OC_{1-4}alkyl, OC_{0-6}alkylaryl, $O(CO)C_{1-4}$alkyl, C_{0-4}alkyl(S)C_{0-4}alkyl, C_{1-4}alkyl(SO)C_{0-4}alkyl, C_{1-4}alkyl(SO_2)C_{0-4}alkyl, (SO)C_{0-4}alkyl, (SO_2)C_{0-4}alkyl, C_{1-4}alkylOR^5, C_{0-4}alkylNR^5R^6 and a 5- or 6-membered ring containing one or more atoms independently selected from C, N, O or S, wherein said ring may be substituted by one or more A;

[0030] R^5 and R^6 are independently selected from the group consisting of hydrogen, hydroxy, C_{1-6}alkyl, C_{0-6}alkylC_{3-6}cycloalkyl, C_{0-6}alkylaryl, C_{0-6}alkylheteroaryl and a 5- or 6-membered ring containing one or more atoms independently selected from C, N, O and S, and wherein R^5 and R^6 may together form a 5- or 6-membered ring containing one or more atoms independently selected from the group consisting of C, N, O and S;

[0031] wherein any C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{0-6}alkylC_{3-6}cycloalkyl, C_{0-6}alkylaryl and C_{0-6}alkylheteroaryl defined under R^1, R^2, R^3, R^4, R^5 and R^6 may be substituted by one or more A;

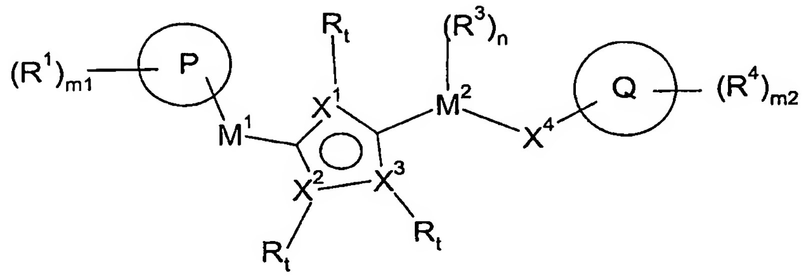
[0032] A is selected from the group consisting of hydrogen, hydroxy, oxo, halo, nitro, C_{0-6}alkylcyano, C_{1-4}alkyl, C_{0-4}alkylC_{3-6}cycloalkyl, C_{1-6}alkylhalo, OC_{1-6}alkylhalo, C_{2-6}alkenyl, OC_{1-6}alkyl, C_{0-3}alkylaryl, C_{0-6}alkylOR^5, OC_{2-6}alkylOR^5, C_{1-6}alkylSR^5, OC_{2-6}alkylSR^5, $(CO)R^5$, $O(CO)R^5$, OC_{2-6}alkylcyano, C_{0-6}alkylCO_2R^5, OC_{1-6}alkylCO_2R^5, $O(CO)OR^5$, OC_{1-6}alkyl$(CO)R^5$, C_{1-6}alkyl$(CO)R^5$, NR^5OR^6, C_{0-6}alkylNR^5R^6, OC_{2-6}alkylNR^5R^6, C_{0-6}alkyl$(CO)NR^5R^6$, OC_{1-6}alkyl$(CO)NR^5R^6$, OC_{2-6}alkyl$NR^5(CO)R^6$, C_{0-6}alkyl$NR^5(CO)R^6$, C_{0-6}alkyl$NR^5(CO)NR^5R^6$, $O(CO)NR^5R^6$, $NR^5(CO)OR^6$, C_{0-6}alkyl$(SO_2)NR^5R^6$, OC_{2-6}alkyl$(SO_2)NR^5R^6$, C_{0-6}alkyl$NR^5(SO_2)R^6$, OC_{2-6}alkyl$NR^5(SO_2)R^6$, SO_3R^5, C_{1-6}alkyl$NR^5(SO_2)NR^5R^6$, OC_{2-6}alkyl$(SO_2)R^5$, C_{0-6}alkyl$(SO_2)R^5$, C_{0-6}alkyl$(SO)R^5$, OC_{2-6}alkyl$(SO)R^5$ and a 5- or 6-membered ring containing one or more atoms independently selected from the group consisting of C, N, O and S;

[0033] m is selected from 0, 1, 2, 3 and 4; and

[0034] n is selected from 0, 1, 2 and 3,

[0035] or salt thereof.

[0036] The present invention provides a compound of formula I



(I)

wherein:

[0037] P is selected from the group consisting of thiophene, pyridyl, thiazolyl, furyl, pyrrolyl and phenyl, whereby the phenyl ring is substituted on position 3 or disubstituted on positions 2 and 5;

[0038] R^1 is attached to P via a carbon atom on ring P and is selected from the group consisting of hydrogen, hydroxy, halo, nitro, C_{1-6}alkylhalo, OC_{1-6}alkylhalo, C_{1-6}alkyl, OC_{1-6}alkyl, C_{2-6}alkenyl, OC_{2-6}alkenyl, C_{2-6}alkynyl, OC_{2-6}alkynyl, C_{0-6}alkylC_{3-6}cycloalkyl, OC_{0-6}alkylC_{3-6}cycloalkyl, C_{0-6}alkylaryl, OC_{0-6}alkylaryl, CHO, (CO)R^5, O(CO)R^5, O(CO)OR^5, O(CN)OR^5, C_{1-6}alkylOR^5, OC_{2-6}alkylOR^5, C_{1-6}alkyl(CO)R^5, OC_{1-6}alkyl(CO)R^5, C_{0-6}alkylCO_2R^5, OC_{1-6}alkylCO_2R^5, C_{0-6}alkylcyano, OC_{2-6}alkylcyano, C_{0-6}alkylNR^5R^6, OC_{2-6}alkylNR^5R^6, C_{1-6}alkyl(CO)NR^5R^6, OC_{1-6}alkyl(CO)NR^5R^6, C_{0-6}alkylNR^5(CO)R^6, OC_{2-6}alkylNR^5(CO)R^6, C_{0-6}alkylNR^5(CO)NR^5R^6, C_{0-6}alkylSR^5, OC_{2-6}alkylSR^5, C_{0-6}alkyl(SO)R^5, OC_{2-6}alkyl(SO)R^5, C_{0-6}alkylSO_2R^5, OC_{2-6}alkylSO_2R^5, C_{0-6}alkyl(SO_2)NR^5R^6, OC_{2-6}alkyl(SO_2)NR^5R^6,C_{0-6}alkylNR^5(SO_2)R^6, OC_{2-6}alkylNR^5(SO_2)R^6, C_{0-6}alkylNR^5(SO_2)NR^5R^6, OC_{2-6}alkylNR^5(SO_2)NR^5R^6, (CO)NR^5R^6, O(CO)NR^5R^6, NR^5OR^6, C_{0-6}alkylNR^5(CO)OR^6, OC_{2-6}alkylNR^5(CO)OR^6, SO_3R^5 and a 5- or 6-membered ring containing one or more atoms independently selected from the group consisting of C, N, O and S;

[0039] M^1 is a bond;

[0040] X^1 selected from the group consisting of C, CO, N, O and S;

[0041] X^2 is selected from the group consisting of C, N, O and S;

[0042] X^3 is i) selected from the group consisting of N, O and S, or

[0043] ii) selected from N, O, S, and C when X^2 is selected from N, O, or S, and

when X^3 is C the substituent R on X^3 is H. ;

[0044] R is selected from the group consisting of hydrogen, C_{0-3}alkyl, halo, C_{0-3}alkylOR^5, C_{0-3}alkylNR^{5}R^6, C_{0-3}alkyl(CO)OR^5 and C_{0-3}alkylaryl;

[0045] M^2 is selected from a group consisting of a bond, C_{1-3}alkyl, C_{2-3}alkynyl, C_{0-4}alkyl(CO)C_{0-4}alkyl, C_{0-3}alkylOC_{0-3}alkyl, C_{0-3}alkylNR^5C_{1-3}alkyl, C_{0-3}alkyl(CO)NR^5, C_{0-4}alkylNR^5, C_{0-3}alkyl(SO)C_{0-3}alkyl and C_{0-3}alkyl(SO_2)C_{0-3}alkyl;

[0046] R^3 is selected from a group consisting of hydroxy, C_{0-6}alkylcyano, oxo, =NR^5, =NOR^5, C_{1-4}alkylhalo, halo, C_{1-4}alkyl, O(CO)C_{1-4}alkyl, C_{1-4}alkyl(SO)C_{0-4}alkyl, C_{1-4}alkyl(SO_2)C_{0-4}alkyl, (SO)C_{0-4}alkyl, (SO_2)C_{0-4}alkyl, OC_{1-4}alkyl, C_{1-4}alkylOR^5 and C_{0-4}alkylNR^{5}R^6;

[0047] X^4 is selected from the group consisting of C_{0-4}alkylR^{5}R^6 , C_{3-7}cycloalkyl, C_{1-4}alkyl(NR^{5}R^6), NR^5, C_{0-4}alkyl(NR^{5}R^6)=N, NR^5C_{0-4}alkyl(NR^{5}R^6)=N, NOC_{0-4}alkyl, C_{1-4}alkylhalo, O, SO, SO_2 and S, and wherein the bond between M^2 and X^4 is a single bond ;

[0048] Q is i) selected from the group consisting of triazolyl, imidazolyl, oxadiazolyl, imidazolonyl, oxazolonyl, thiazolonyl, tetrazolyl and thiadiazolyl, and wherein any substitutable nitrogen atom in the ring is substituted with R^4 on such nitrogen atom and any suitable carbon atom is optionally substituted with R^4; and

[0049] R^4 is selected from the group consisting of C_{0-6}alkylcyano, =NC_{1-4}alkyl, =NOR^5, C_{1-4}alkylhalo, halo, C_{1-6}alkyl, OC_{1-4}alkyl, C_{2-4}alkenyl, C_{0-2}alkylC_{3-6}cycloalkyl, C_{0-6}alkylaryl, C_{0-6}alkylheteroaryl, OC_{0-6}alkylaryl, OC_{0-6}alkylheteroaryl, NC_{0-6}alkylaryl, NC_{0-6}alkylheteroaryl,C_{0-6}alkylOaryl, C_{0-6}alkylOheteroaryl, C_{0-6}alkylNaryl, C_{0-6}alkylNheteroaryl, OC_{0-6}alkylOaryl, OC_{0-6}alkylOheteroaryl, OC_{0-6}alkylNaryl, OC_{0-6}alkylNheteroaryl, NC_{0-6}alkylOaryl, NC_{0-6}alkylOheteroaryl, NC_{0-6}alkylNaryl, NC_{0-6}alkylNheteroaryl, O(CO)C_{1-4}alkyl, C_{0-4}alkyl(CO)OC_{1-4}alkyl, C_{1-4}alkyl(S)C_{0-4}alkyl, C_{1-4}alkyl(SO)C_{0-4}alkyl, C_{1-4}alkyl(SO_2)C_{0-4}alkyl, (SO)C_{0-4}alkyl, (SO_2)C_{0-4}alkyl, C_{1-4}alkylOR^5, C_{0-4}alkylN(C_{1-4}alkyl)$_2$ and a 3- or 6-membered non-aromatic ring containing one or more atoms independently selected from C, N, O and S, which ring may optionally be fused with a 5-membered ring containing one or more atoms independently selected from the group consisting of C, N and O and wherein said ring and said fused ring

may be substituted by one or two A; or

[0050] ii) selected from the group consisting of benzoimidazolyl, benzooxazolyl, tetrahydrotriazolopyridyl, tetrahydrotriazolopyrimidinyl, pyridonyl, pyridazinyl, imidazopyridyl, oxazolopyridyl, thiazolopyridyl, imidazopyridazinyl, oxazolopyridazinyl, thiazolopyridazinyl and purinyl; and

[0051] R^4 is selected from the group consisting of hydrogen, hydroxy, C_{0-6}alkylcyano, $=NR^5$, $=NOR^5$, C_{1-4}alkylhalo, halo, C_{1-6}alkyl, OC_{1-4}alkyl, OC_{0-6}alkylaryl, $O(CO)C_{1-4}$alkyl, C_{0-4}alkyl(S)C_{0-4}alkyl, C_{1-4}alkyl(SO)C_{0-4}alkyl, C_{1-4}alkyl(SO_2)C_{0-4}alkyl, (SO)C_{0-4}alkyl, (SO_2)C_{0-4}alkyl, C_{1-4}alkylOR^5, C_{0-4}alkylNR^5R^6 and a 5- or 6-membered ring containing one or more atoms independently selected from C, N, O and S, which ring may optionally be fused with a 5- or 6-membered ring containing one or more atoms independently selected from the group consisting of C, N and O and wherein said ring and said fused ring may be substituted by one or two A;

[0052] R^5 and R^6 are independently selected from the group consisting of hydrogen and C_{1-6}alkyl;

wherein any C_{1-6}alkyl defined under R^1, R^2 and R^4 may be substituted by one or more A;

[0053] A is selected from the group consisting of hydrogen, hydroxy, halo, nitro, oxo, C_{0-6}alkylcyano, C_{0-4}alkylC_{3-6}cycloalkyl, C_{1-6}alkyl, C_{1-6}alkylhalo, OC_{1-6}alkylhalo, C_{2-6}alkenyl, C_{0-3}alkylaryl, C_{0-6}alkylOR^5, OC_{2-6}alkylOR^5, C_{1-6}alkylSR^5, OC_{2-6}alkylSR^5, $(CO)R^5$, $O(CO)R^5$, OC_{2-6}alkylcyano, OC_{1-6}alkylCO_2R^5, $O(CO)OR^5$, OC_{1-6}alkyl$(CO)R^5$, C_{1-6}alkyl$(CO)R^5$, NR^5OR^6, OC_{2-6}alkylNR^5R^6, C_{0-6}alkyl$(CO)NR^5R^6$, OC_{1-6}alkyl$(CO)NR^5R^6$, OC_{2-6}alkyl$NR^5(CO)R^6$, C_{0-6}alkyl$NR^5(CO)R^6$, C_{0-6}alkyl$NR^5(CO)NR^5R^6$, $O(CO)NR^5R^6$, C_{0-6}alkyl$(SO_2)NR^5R^6$, OC_{2-6}alkyl$(SO_2)NR^5R^6$, C_{0-6}alkyl$NR^5(SO_2)R^6$, OC_{2-6}alkyl$NR^5(SO_2)R^6$, SO_3R^5, C_{1-6}alkyl$NR^5(SO_2)NR^5R^6$, OC_{2-6}alkyl$(SO_2)R^5$, C_{0-6}alkyl$(SO_2)R^5$, C_{0-6}alkyl$(SO)R^5$, OC_{2-6}alkyl$(SO)R^5$ and a 5-membered ring containing one or more atoms independently selected from the group consisting of C, N, O and S;

[0054] m1 is selected from 0, 1, 2, 3 and 4;

[0055] m2 is selected from 0, 1, 2 and 3;

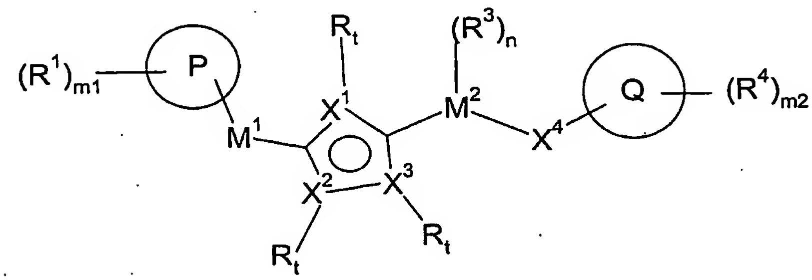
[0056] n is selected from 0, 1 and 2; and

[0057] t is 0 or 1,

[0058] and salts thereof,

[0059] with the proviso that the compound is not 5-(4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-thiophen-3-yl-[1,2,4]oxadiazole, 1,2-di{2-(3-amino-phenyl)-[1,3,4]oxadiazole-yl)ethane, 1,2-di{5-[5-(4-nitro-phenyl)furan-2-yl]-[1,3,4]oxadiazol-yl)ethane, 1,2-di{5-[5-(4-bromo-phenyl)furan-2-yl]-[1,3,4]oxadiazol-yl)ethane, 1,2-di{5-[5-(4-chloro-phenyl)furan-2-yl]-[1,3,4]oxadiazol-yl)ethane and 1,2-di{5-[5-(2,4-dibromo-phenyl)furan-2-yl]-[1,3,4]oxadiazol-yl)ethane.

[0060] The present invention provides a compound of formula Ib



(Ib)

wherein:

[0061] P is selected from the group consisting of thiophene, pyridyl, thiazolyl, furyl, pyrrolyl and phenyl, whereby the phenyl ring is substituted on position 3 or disubstituted on positions 2 and 5;

[0062] R^1 is attached to P via a carbon atom on ring P and is selected from the group consisting of hydrogen, hydroxy, halo, nitro, C_{1-6}alkylhalo, OC_{1-6}alkylhalo, C_{1-6}alkyl, OC_{1-6}alkyl, C_{2-6}alkenyl, OC_{2-6}alkenyl, C_{2-6}alkynyl, OC_{2-6}alkynyl, C_{0-6}alkylC_{3-6}cycloalkyl, OC_{0-6}alkylC_{3-6}cycloalkyl, C_{0-6}alkylaryl, OC_{0-6}alkylaryl, CHO, $(CO)R^5$, $O(CO)R^5$, $O(CO)OR^5$, $O(CN)OR^5$, C_{1-6}alkylOR^5, OC_{2-6}alkylOR^5, C_{1-6}alkyl$(CO)R^5$, OC_{1-6}alkyl$(CO)R^5$, C_{0-6}alkylCO_2R^5, OC_{1-6}alkylCO_2R^5, C_{0-6}alkylcyano, OC_{2-6}alkylcyano, C_{0-6}alkylNR^5R^6, OC_{2-6}alkylNR^5R^6, C_{1-6}alkyl$(CO)NR^5R^6$, OC_{1-6}alkyl$(CO)NR^5R^6$, C_{0-6}alkyl$NR^5(CO)R^6$, OC_{2-6}alkyl$NR^5(CO)R^6$, C_{0-6}alkyl$NR^5(CO)NR^5R^6$, C_{0-6}alkylSR^5, OC_{2-6}alkylSR^5, C_{0-6}alkyl$(SO)R^5$, OC_{2-6}alkyl$(SO)R^5$, C_{0-6}alkylSO_2R^5, OC_{2-6}alkylSO_2R^5, C_{0-6}alkyl$(SO_2)NR^5R^6$, OC_{2-}

${}_{6}$alkyl(SO_2)NR^5R^6,C_{0-6}alkylNR^5(SO_2)R^6, OC_{2-6}alkylNR^5(SO_2)R^6, C_{0-6}alkylNR^5(SO_2)NR^5R^6, OC_{2-6}alkylNR^5(SO_2)NR^5R^6, (CO)NR^5R^6, O(CO)NR^5R^6, NR^5OR^6, C_{0-6}alkylNR^5(CO)OR^6, OC_{2-6}alkylNR^5(CO)OR^6, SO_3R^5 and a 5- or 6-membered ring containing one or more atoms independently selected from the group consisting of C, N, O and S;

[0063] M^1 is a bond;

[0064] X^1 selected from the group consisting of C, CO, N, O and S;

[0065] X^2 is selected from the group consisting of C, N, O and S;

[0066] X^3 is selected from the group consisting of N, O and S, or X^3 is CH when X^2 is N, O or S;

[0067] R is selected from the group consisting of hydrogen, C_{0-3}alkyl, halo, C_{0-3}alkylOR^5, C_{0-3}alkylNR^5R^6, C_{0-3}alkyl(CO)OR^5 and C_{0-3}alkylaryl;

[0068] M^2 is selected from a group consisting of a bond, C_{1-3}alkyl, C_{2-3}alkynyl, C_{0-4}alkyl(CO)C_{0-4}alkyl, C_{0-3}alkylOC_{0-3}alkyl, C_{0-3}alkylNR^5C_{1-3}alkyl, C_{0-3}alkyl(CO)NR^5, C_{0-4}alkylNR^5, C_{0-3}alkyl(SO)C_{0-3}alkyl and C_{0-3}alkyl(SO_2)C_{0-3}alkyl;

[0069] R^3 is selected from a group consisting of hydroxy, C_{0-6}alkylcyano, oxo, $=NR^5$, $=NOR^5$, C_{1-4}alkylhalo, halo, C_{1-4}alkyl, O(CO)C_{1-4}alkyl, C_{1-4}alkyl(SO)C_{0-4}alkyl, C_{1-4}alkyl(SO_2)C_{0-4}alkyl, (SO)C_{0-4}alkyl, (SO_2)C_{0-4}alkyl, OC_{1-4}alkyl, C_{1-4}alkylOR^5 and C_{0-4}alkylNR^5R^6;

[0070] X^4 is selected from the group consisting of C_{0-4}alkylR^5R^6, C_{3-7}cycloalkyl, C_{1-4}alkyl(NR^5R^6), NR^5, C_{0-4}alkyl(NR^5R^6)=N, NR^5C_{0-4}alkyl(NR^5R^6)=N, NOC_{0-4}alkyl, C_{1-4}alkylhalo, O, SO, SO_2 and S, and wherein the bond between M^2 and X^4 is a single bond ;

[0071] Q is i) selected from the group consisting of triazolyl, imidazolyl, oxadiazolyl, imidazolonyl, oxazolonyl, thiazolonyl, tetrazolyl and thiadiazolyl, and wherein any substitutable nitrogen atom in the ring is substituted with R^4 on such nitrogen atom; and

[0072] R^4 is selected from the group consisting of C_{0-6}alkylcyano, $=NC_{1-4}$alkyl, $=NOR^5$, C_{1-4}alkylhalo, halo, C_{1-6}alkyl, OC_{1-4}alkyl, C_{2-4}alkenyl, C_{0-2}alkylC_{3-6}cycloalkyl, C_{0-6}alkylaryl, C_{0-6}alkylheteroaryl, OC_{0-6}alkylaryl, OC_{0-6}alkylheteroaryl, NC_{0-6}alkylaryl, NC_{0-6}alkylheteroaryl,C_{0-6}alkylOaryl, C_{0-}

$_{6}$alkylOheteroaryl, C_{0-6}alkylNaryl, C_{0-6}alkylNheteroaryl, OC_{0-6}alkylOaryl, OC_{0-6}alkylOheteroaryl, OC_{0-6}alkylNaryl, OC_{0-6}alkylNheteroaryl, NC_{0-6}alkylOaryl, NC_{0-6}alkylOheteroaryl, NC_{0-6}alkylNaryl, NC_{0-6}alkylNheteroaryl, $O(CO)C_{1-4}$alkyl, C_{0-4}alkyl$(CO)OC_{1-4}$alkyl, C_{1-4}alkyl$(S)C_{0-4}$alkyl, C_{1-4}alkyl$(SO)C_{0-4}$alkyl, C_{1-4}alkyl$(SO_2)C_{0-4}$alkyl, $(SO)C_{0-4}$alkyl, $(SO_2)C_{0-4}$alkyl, C_{1-4}alkylOR^5, C_{0-4}alkyl$N(C_{1-4}$alkyl$)_2$ and a 3- or 6-membered non-aromatic ring containing one or more atoms independently selected from C, N, O and S, which ring may optionally be fused with a 5-membered ring containing one or more atoms independently selected from the group consisting of C, N and O and wherein said ring and said fused ring may be substituted by one or two A; or

[0073] ii) selected from the group consisting of benzoimidazolyl, benzooxazolyl, tetrahydrotriazolopyridyl, tetrahydrotriazolopyrimidinyl, pyridonyl, pyridazinyl, imidazopyridyl, oxazolopyridyl, thiazolopyridyl, imidazopyridazinyl, oxazolopyridazinyl, thiazolopyridazinyl and purinyl; and

[0074] R^4 is selected from the group consisting of hydrogen, hydroxy, C_{0-6}alkylcyano, $=NR^5$, $=NOR^5$, C_{1-4}alkylhalo, halo, C_{1-6}alkyl, OC_{1-4}alkyl, OC_{0-6}alkylaryl, $O(CO)C_{1-4}$alkyl, C_{0-4}alkyl$(S)C_{0-4}$alkyl, C_{1-4}alkyl$(SO)C_{0-4}$alkyl, C_{1-4}alkyl$(SO_2)C_{0-4}$alkyl, $(SO)C_{0-4}$alkyl, $(SO_2)C_{0-4}$alkyl, C_{1-4}alkylOR^5, C_{0-4}alkylNR^5R^6 and a 5- or 6-membered ring containing one or more atoms independently selected from C, N, O and S, which ring may optionally be fused with a 5- or 6-membered ring containing one or more atoms independently selected from the group consisting of C, N and O and wherein said ring and said fused ring may be substituted by one or two A;

[0075] R^5 and R^6 are independently selected from the group consisting of hydrogen and C_{1-6}alkyl;

[0076] wherein any C_{1-6}alkyl defined under R^1, R^2 and R^4 may be substituted by one or more A;

[0077] A is selected from the group consisting of hydrogen, hydroxy, halo, nitro, oxo, C_{0-6}alkylcyano, C_{0-4}alkylC_{3-6}cycloalkyl, C_{1-6}alkyl, C_{1-6}alkylhalo, OC_{1-6}alkylhalo, C_{2-6}alkenyl, C_{0-3}alkylaryl, C_{0-6}alkylOR^5, OC_{2-6}alkylOR^5, C_{1-6}alkylSR^5, OC_{2-6}alkylSR^5, $(CO)R^5$, $O(CO)R^5$, OC_{2-6}alkylcyano, OC_{1-6}alkylCO_2R^5, $O(CO)OR^5$, OC_{1-}

$_6$alkyl(CO)R^5, C_{1-6}alkyl(CO)R^5, NR^5OR^6, OC_{2-6}alkylNR^5R^6, C_{0-6}alkyl(CO)NR^5R^6, OC_{1-6}alkyl(CO)NR^5R^6, OC_{2-6}alkylNR^5(CO)R^6, C_{0-6}alkylNR^5(CO)R^6, C_{0-6}alkylNR^5(CO)NR^5R^6, O(CO)NR^5R^6, C_{0-6}alkyl(SO_2)NR^5R^6, OC_{2-6}alkyl(SO_2)NR^5R^6, C_{0-6}alkylNR^5(SO_2)R^6, OC_{2-6}alkylNR^5(SO_2)R^6, SO_3R^5, C_{1-6}alkylNR^5(SO_2)NR^5R^6, OC_{2-6}alkyl(SO_2)R^5, C_{0-6}alkyl(SO_2)R^5, C_{0-6}alkyl(SO)R^5, OC_{2-6}alkyl(SO)R^5 and a 5-membered ring containing one or more atoms independently selected from the group consisting of C, N, O and S;

[0078] m1 is selected from 0, 1, 2, 3 and 4;

[0079] m2 is selected from 0, 1, 2 and 3;

[0080] n is selected from 0, 1 and 2; and

[0081] t is 0 or 1,

[0082] and salts thereof,

[0083] with the proviso that the compound is not 5-(4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-thiophen-3-yl-[1,2,4]oxadiazole.

[0084] In a further aspect of the invention there is provided pharmaceutical formulations comprising a therapeutically effective amount of a compound of formula I and a pharmaceutically acceptable carrier.

[0085] In yet a further aspect of the invention there is provided a pharmaceutical formulation including a compound of formula I for use in the treatment of mGluR5 receptor-mediated disorders, and particularly neurological disorders, psychiatric disorders, acute and chronic pain, and gastrointestinal disorders.

[0086] In still a further aspect of the invention there is provided a compound of formula I for use in therapy for the treatment of mGluR5 receptor-mediated disorders, and particularly neurological disorders, psychiatric disorders, acute and chronic pain, and gastrointestinal disorders.

[0087] In another aspect of the invention there is provided a process for the preparation of compounds of formula I, and the intermediates provided therein.

[0088] These and other aspects of the present invention are described in greater detail herein below.

DETAILED DESCRIPTION OF THE INVENTION

[0089] Listed below are definitions of various terms used in the specification and claims to describe the present invention.

[0090] For the avoidance of doubt it is to be understood that where in this specification a group is qualified by 'hereinbefore defined', 'defined hereinbefore' or 'defined above' the said group encompasses the first occurring and broadest definition as well as each and all of the other definitions for that group.

[0091] For the avoidance of doubt it is to be understood that in this specification 'C_{1-6}' means a carbon group having 1, 2, 3, 4, 5 or 6 carbon atoms.

[0092] In this specification "C" means 1 carbon atom.

[0093] In this specification, unless stated otherwise, the term "alkyl" includes both straight and branched chain alkyl groups and may be methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl,

[0094] s-butyl, t-butyl, n-pentyl, i-pentyl, t-pentyl, neo-pentyl, n-hexyl or i-hexyl, t-hexyl. The term "C_{1-3}alkyl" refers to an alkyl group having 1, 2 or 3 carbon atoms, and may be methyl, ethyl, n-propyl and i-propyl.

[0095] In this specification, unless stated otherwise, the term "cycloalkyl" refers to an optionally substituted, saturated cyclic hydrocarbon ring system. The term "C_{3-7}cycloalkyl" may be cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl and cycloheptyl.

[0096] In this specification, unless stated otherwise, the term "alkenyl" includes both straight and branched chain alkenyl groups. The term "C_{2-6}alkenyl" refers to an alkenyl group having 2 to 6 carbon atoms and one or two double bonds, and may be, but is not limited to vinyl, allyl, propenyl, i-propenyl, butenyl, i-butenyl, crotyl, pentenyl, i-pentenyl and hexenyl.

[0097] In this specification, unless stated otherwise, the term "alkynyl" includes both straight and branched chain alkynyl groups. The term C_{2-6}alkynyl having 2 to 6 carbon atoms and one or two triple bonds, and may be, but is not limited to ethynyl, propargyl, butynyl, i-butynyl, pentynyl, i-pentynyl and hexynyl.

[0098] The term "aryl" refers to an optionally substituted monocyclic or bicyclic

hydrocarbon ring system containing at least one unsaturated aromatic ring. Examples and suitable values of the term "aryl" are phenyl, naphthyl, 1,2,3,4-tetrahydronaphthyl, indyl and indenyl.

[0099] In this specification, unless stated otherwise, the term "heteroaryl" refer to an optionally substituted monocyclic or bicyclic unsaturated, aromatic ring system containing at least one heteroatom selected independently from N, O or S. Examples of "heteroaryl" may be, but are not limited to thiophene, thienyl, pyridyl, thiazolyl, furyl, pyrrolyl, triazolyl, imidazolyl, oxadiazolyl, oxazolyl, isoxazolyl, pyrazolyl, imidazolonyl, oxazolonyl, thiazolonyl, tetrazolyl and thiadiazolyl, benzoimidazolyl, benzooxazolyl, tetrahydrotriazolopyridyl, tetrahydrotriazolopyrimidinyl, benzofuryl, indolyl, isoindolyl, pyridonyl, pyridazinyl, pyrimidinyl, imidazopyridyl, oxazolopyridyl, thiazolopyridyl, pyridyl, imidazopyridazinyl, oxazolopyridazinyl, thiazolopyridazinyl and purinyl.

[0100] In this specification, unless stated otherwise, the term "alkylaryl", "alkylheteroaryl " and "alkylcycloalkyl " refer to a substituent that is attached via the alkyl group to an aryl, heteroaryl and cycloalkyl group.

[0101] In this specification, unless stated otherwise, a 5- or 6-membered ring containing one or more atoms independently selected from C, N, O or S, includes aromatic and heteroaromatic rings as well as carbocyclic and heterocyclic rings which may be saturated or unsaturated. Examples of such rings may be, but are not limited to furyl, isoxazolyl, isothiazolyl, oxazolyl, pyrazinyl, pyrazolyl, pyridazinyl, pyridyl, pyrimidyl, pyrrolyl, thiazolyl, thienyl, imidazolyl, imidazolidinyl, imidazolinyl, triazolyl, morpholinyl, piperazinyl, piperidyl, piperidonyl, pyrazolidinyl, pyrazolinyl, pyrrolidinyl, pyrrolinyl, tetrahydropyranyl, thiomorpholinyl, phenyl, cyclohexyl, cyclopentyl and cyclohexenyl.

[0102] In this specification, unless stated otherwise, a 3- to 8-membered ring containing one or more atoms independently selected from C, N, O or S, includes aromatic and heteroaromatic rings as well as carbocyclic and heterocyclic rings which may be saturated or unsaturated. Examples of such rings may be, but are not limited to imidazolidinyl, imidazolinyl, morpholinyl, piperazinyl, piperidyl, piperidonyl, pyrazolidinyl, pyrazolinyl, pyrrolidinyl, pyrrolinyl, tetrahydropyranyl or

thiomorpholinyl, tetrahydrothiopyranyl, furyl, pyrrolyl, isoxazolyl, isothiazolyl, oxazolyl, oxazolidinonyl, pyrazinyl, pyrazolyl, pyridazinyl, pyridyl, pyrimidyl, pyrrolyl, thiazolyl, thienyl, imidazolyl, triazolyl, phenyl, cyclopropyl, aziridinyl, cyclobutyl, azetidinyl, cyclopentyl, cyclopentenyl, cyclohexyl, cyclohexenyl, cycloheptyl, cycloheptenyl, cyclooctyl and cyclooctenyl.

[0103] In this specification, unless stated otherwise, a 3- to 8-membered ring containing one or more atoms independently selected from C, N, O or S, which group may optionally be fused with a 5- or 6-membered ring containing one or more atoms independently selected from C, N, O or S, includes aromatic and heteroaromatic rings as well as carbocyclic and heterocyclic rings which may be saturated or unsaturated. Examples of such rings may be, but are not limited to naphthyl, norcaryl, chromyl, isochromyl, indanyl, benzoimidazol or tetralinyl, benzooxazolyl, benzothiazolyl, benzofuryl, benzothienyl, benzotriazolyl, indolyl, azaindolyl, indazolyl, indolinyl, isoindolinyl, benzimidazolyl, oxadiazolyl, thiadiazolyl, quinolinyl, quinoxalinyl and benzotriazolyl.

[0104] In this specification, unless stated otherwise, the term "$=NR^5$" and "$=NOR^5$" include imino- and oximogroups carrying an R^5 substituent and may be, or be part of, groups including, but not limited to iminoalkyl, iminohydroxy, iminoalkoxy, amidine, hydroxyamidine and alkoxyamidine.

[0105] In the case where a subscript is the integer 0 (zero) the group to which the subscript refers, indicates that the group is absent, i.e. there is a direct bond between the groups.

[0106] In this specification, unless stated otherwise, the term "bond" is a saturated bond.

[0107] In this specification, unless stated otherwise, the term "halo" may be fluoro, chloro, bromo or iodo.

[0108] In this specification, unless stated otherwise, the term "alkylhalo" means an alkyl group as defined above, substituted with one or more halo. The term "C_{1-6}alkylhalo" may include, but is not limited to fluoromethyl, difluoromethyl, trifluoromethyl, fluoroethyl, difluoroethyl and bromopropyl. The term "OC_{1-6}alkylhalo" may include, but is not limited to fluoromethoxy, difluoromethoxy,

trifluoromethoxy, fluoroethoxy and difluoroethoxy.

[0109] In one embodiments of the invention P may be hydrogen or C_{3-7} alkyl or P may be a 3- to 8-membered ring containing one or more atoms selected from C, N, O or S said ring may be optionally fused with a 5- or 6-membered ring containing one or more atoms independently selected from C, N, O, or S. In a preferred embodiment of the invention P is selected from 5 and 6 membered aromatic and heteroaromatic rings.

[0110] In a further preferred embodiment P is selected from thiophene, pyridyl, thiazolyl, furyl, pyrrolyl and phenyl, whereby the phenyl ring is substituted on position 3 or disubstituted on positions 2 and 5.

[0111] In yet a further preferred embodiment of the invention P is phenyl substituted on position 3 or disubstituted on positions 2 and 5.

[0112] P is optionally substituted via a carbon atom with 0, 1, 2, 3 or 4 groups R^1, wherein the number of R^1 substituents on the P ring is designated by the term *m1*. In preferred embodiments of the invention *m1* is 1 or 2. In further preferred embodiments of the invention *m1* is 1.

[0113] In suitable embodiments of invention R^1 is selected from the group consisting of hydrogen, hydroxy, halo, nitro, C_{1-6}alkylhalo, OC_{1-6}alkylhalo, C_{1-6}alkyl, OC_{1-6}alkyl, C_{2-6}alkenyl, OC_{2-6}alkenyl, C_{2-6}alkynyl, OC_{2-6}alkynyl, C_{0-6}alkylC_{3-6}cycloalkyl, OC_{0-6}alkylC_{3-6}cycloalkyl, C_{0-6}alkylaryl, OC_{0-6}alkylaryl, CHO, $(CO)R^5$, $O(CO)R^5$, $O(CO)OR^5$, $O(CN)OR^5$, C_{1-6}alkylOR^5, OC_{2-6}alkylOR^5, C_{1-6}alkyl$(CO)R^5$, OC_{1-6}alkyl$(CO)R^5$, C_{0-6}alkylCO_2R^5, OC_{1-6}alkylCO_2R^5, C_{0-6}alkylcyano, OC_{2-6}alkylcyano, C_{0-6}alkylNR^5R^6, OC_{2-6}alkylNR^5R^6, C_{1-6}alkyl$(CO)NR^5R^6$, OC_{1-6}alkyl$(CO)NR^5R^6$, C_{0-6}alkyl$NR^5(CO)R^6$, OC_{2-6}alkyl$NR^5(CO)R^6$, C_{0-6}alkyl$NR^5(CO)NR^5R^6$, C_{0-6}alkylSR^5, OC_{2-6}alkylSR^5, C_{0-6}alkyl$(SO)R^5$, OC_{2-6}alkyl$(SO)R^5$, C_{0-6}alkylSO_2R^5, OC_{2-6}alkylSO_2R^5, C_{0-6}alkyl$(SO_2)NR^5R^6$, OC_{2-6}alkyl$(SO_2)NR^5R^6$,C_{0-6}alkyl$NR^5(SO_2)R^6$, OC_{2-6}alkyl$NR^5(SO_2)R^6$, C_{0-6}alkyl$NR^5(SO_2)NR^5R^6$, OC_{2-6}alkyl$NR^5(SO_2)NR^5R^6$, $(CO)NR^5R^6$, $O(CO)NR^5R^6$, NR^5OR^6, C_{0-6}alkyl$NR^5(CO)OR^6$, OC_{2-6}alkyl$NR^5(CO)OR^6$, SO_3R^5 and a 5- or 6-membered ring containing one or more atoms independently selected from the group consisting of C, N, O and S.

[0114] In a more suitable embodiment of the invention R^1 is selected from

hydrogen, hydroxy, halo, nitro, C_{1-6}alkylhalo, OC_{1-6}alkylhalo, C_{1-6}alkyl, OC_{1-5}alkyl, C_{2-6}alkenyl, C_{0-6}alkylC_{3-6}cycloalkyl, C_{1-6}alkylOR^5, C_{1-6}alkyl(CO)R^5, C_{0-6}alkylCO_2R^5, C_{0-6}alkylcyano, C_{0-6}alkylNR^5R^6, C_{0-6}alkylSR^5 and a 5- or 6-membered ring containing one or more atoms independently selected from the group consisting of C and O.

[0115] Any C_{1-6}alkyl defined under R^1 may be substituted by one or more A. In one embodiment of the invention R^1 is ethyl and A is hydroxyl.

[0116] In a further suitable embodiment of the invention R^1 is selected from hydrogen, methyl, ethyl, cyclopropyl, hydroxy, methoxy, cyano, flouro, chloro, bromo, iodo, trifluoromethyl, difluoromethoxy, trifluoromethoxy, amino, nitro, dimethylamino, methylsulfanyl, vinyl, acetyl, formic acid methyl ester, methoxymethyl, ethanol and furyl.

[0117] In a more suitable embodiment of the invention P is selected from the group consisting of thiophene, pyridyl, thiazolyl, furyl, pyrrolyl or phenyl, whereby the phenyl ring is substituted on position 3 or disubstituted on positions 2 and 5 and R^1 is selected from the group consisting of hydrogen, hydroxy, halo, nitro, C_{1-6}alkylhalo, OC_{1-6}alkylhalo, C_{1-6}alkyl, OC_{1-6}alkyl, C_{2-6}alkenyl, C_{0-6}alkylC_{3-6}cycloalkyl, C_{1-6}alkylOR^5, C_{1-6}alkyl(CO)R^5, C_{0-6}alkylCO_2R^5, C_{0-6}alkylcyano, C_{0-6}alkylNR^5R^6, C_{0-6}alkylSR^5 and a 5-membered ring containing one or more atoms independently selected from the group consisting of C and O.

[0118] In a further suitable embodiment of the invention P is phenyl substituted on position 3 or disubstituted on positions 2 and 5 and R^1 is selected from the group consisting of hydrogen, hydroxy, halo, nitro, C_{1-6}alkylhalo, OC_{1-6}alkylhalo, C_{1-6}alkyl, OC_{1-6}alkyl, C_{2-6}alkenyl, C_{0-6}alkylC_{3-6}cycloalkyl, C_{1-6}alkylOR^5, C_{1-6}alkyl(CO)R^5, C_{0-6}alkylCO_2R^5, C_{0-6}alkylcyano, C_{0-6}alkylNR^5R^6, C_{0-6}alkylSR^5 and a 5-membered ring containing one or more atoms independently selected from the group consisting of C and O.

[0119] According to another aspect of the invention the ring P is connected to the core ring by M^1, wherein M^1 can be a bond directly joining P to the core ring. M^1 can also be a linker C_{1-3}alkyl.

[0120] In a preferred embodiment of the invention M^1 is a bond.

[0121] When M^1 is not a direct bond M^1 can be further substituted with 0, 1, 2 or 3

substituents R^2 wherein the number of substituents R^2 is designated by the term *n*. The substituents R^2 may be selected from hydrogen, hydroxy, oxo, C_{1-4}alkylhalo, halo and C_{1-4}alkyl. In a preferred embodiment of the invention *n* is 0.

[0122] In another aspect of the invention there is provided compounds of formula I wherein X^1 is selected from the group consisting of C, CO, N, O and S. In a further aspect of the invention X^2 is selected from the group consisting of C, N, O and S. In yet a further aspect of the invention X^3 is selected from the group consisting of N, O and S, or X^3 is selected from N, O, S, and C when X^2 is selected from N, O, or S, and when X^3 is C the substituent R on X^3 is H.

[0123] X^1, X^2 and X^3 can be further substituted with 0, 1 or 2 substituents R wherein the number of substituents R is designated by the term *t*. The substituent R may be selected from the group consisting of hydrogen, C_{0-3}alkyl, halo, C_{0-3}alkylOR^5, C_{0-3}alkylNR^{5}R^6, C_{0-3}alkyl(CO)OR^5, C_{0-3}alkylNR^{5}R^6 and C_{0-3}alkylaryl. In one embodiment of the invention R is selected from the group consisting of hydrogen, C_{0-3}alkyl and halo.

[0124] In a preferred embodiment of the invention X^1 is C, N or O and R is selected from hydrogen, C_{0-3}alkyl and halo. In one embodiment R is selected from hydrogen, chloro or methyl.

[0125] In another preferred embodiment of the invention X^1 is N.

[0126] In a suitable embodiment X^2 is selected from N, O and S, and R is hydrogen. In another embodiment of the invention X^3 is N, O or S. In a further preferred embodiment of the invention X^1 is O and one of X^2 and X^3 is O and the other is N. In yet a further preferred embodiment of the invention X^1 is N and one of X^2 and X^3 is O and the other is N. In yet another preferred embodiment of the invention X^1 is C or CR and one of X^2 and X^3 is O and the other is N.

[0127] In another preferred embodiment of the invention X^2 is O and X^3 is N, and in yet another preferred embodiment of the invention X^2 is N and X^3 is O.

[0128] In a further preferred embodiment of the invention X^1 is O and X^2 and X^3 are N.

[0129] In another suitable embodiment of the invention the ring containing X^1, X^2 and X^3 forms an oxadiazole, isoxazole, oxazole, chloro-isoxazole or a methyl-

isoxazole.

[0130] In a preferred embodiment of the invention the ring containing X^1, X^2 and X^3 forms an oxadiazole. In another preferred embodiment of the invention the ring containing X^1, X^2 and X^3 forms an isoxazole.

[0131] The ring containing X^1, X^2 and X^3 should not be further annulated onto any other ring.

[0132] In a suitable embodiment of the invention M^2 may be a direct bond from the core ring to the variable X^4 or M^2 may be selected from the group consisting of bond, C_{1-3}alkyl, C_{2-3}alkynyl, C_{0-4}alkyl(CO)C_{0-4}alkyl, C_{0-3}alkylOC_{0-3}alkyl, C_{0-3}alkylNR^5C_{1-3}alkyl, C_{0-3}alkyl(CO)NR^5, C_{0-4}alkylNR^5, C_{0-3}alkyl(SO)C_{0-3}alkyl and C_{0-3}alkyl(SO_2)C_{0-3}alkyl.

[0133] In preferred embodiments of the invention M^2 is a bond or C_{1-3}alkyl. In further preferred embodiments of the invention M^2 is C_{1-3}alkyl, preferably methyl or ethyl.

[0134] When M_2 is not a direct bond M^2 may be further substituted with 0, 1 or 2 R^3 groups wherein the number of substituents R^3 is designated by the term *n*. In one embodiment of the invention *n* is 1 or 2. In another embodiment of the invention *n* is 0.

[0135] In a suitable embodiment of the invention R^3 is selected from the group consisting of R^3 is selected from a group consisting of hydroxy, C_{0-6}alkylcyano, oxo, $=NR^5$, $=NOR^5$, C_{1-4}alkylhalo, halo, C_{1-4}alkyl, O(CO)C_{1-4}alkyl, C_{1-4}alkyl(SO)C_{0-4}alkyl, C_{1-4}alkyl(SO_2)C_{0-4}alkyl, (SO)C_{0-4}alkyl, (SO_2)C_{0-4}alkyl, OC_{1-4}alkyl, C_{1-4}alkylOR^5 and C_{0-4}alkylNR^5R^6.

[0136] In a preferred embodiment R^3 is selected from hydrogen and C_{1-4}alkyl, preferably methyl or dimethyl.

[0137] In another preferred embodiment M^2 may be selected from the group consisting of a bond, C_{1-3}alkyl, C_{2-3}alkynyl, C_{0-4}alkyl(CO)C_{0-4}alkyl, C_{0-3}alkylOC_{0-3}alkyl, C_{0-3}alkylNR^5C_{1-3}alkyl, C_{0-3}alkyl(CO)NR^5, C_{0-4}alkylNR^5, C_{0-3}alkyl(SO)C_{0-3}alkyl and C_{0-3}alkyl(SO_2)C_{0-3}alkyl and R^3 is selected from hydrogen and C_{1-4}alkyl.

[0138] In yet another preferred embodiments of the invention M^2 is a bond or C_{1-3}alkyl and R^3 is hydrogen, methyl or dimethyl.

[0139] In a further preferred embodiment M^2 may be selected from the group consisting of a bond, methyl and ethyl and R^3 is hydrogen, methyl or dimethyl.

[0140] In a further embodiment of the invention M^2 is nitrogen. In yet a further embodiment of the invention M^2 is oxygen.

[0141] According to another aspect of the invention X^4 is selected from the group consisting of $C_{0-4}alkylR^5R^6$, C_{3-7}cycloalkyl, $C_{1-4}alkyl(NR^5R^6)$, NR^5, $C_{0-4}alkyl(NR^5R^6)$=N, $NR^5C_{0-4}alkyl(NR^5R^6)$=N, NOC_{0-4}alkyl, C_{1-4}alkylhalo, O, SO, SO_2 and S, and wherein the bond between M^2 and X^4 is a single bond.

[0142] In a preferred embodiment of the invention X^4 is selected from the group consisting of $C_{0-4}alkylR^5R^6$, C_{3-7}cycloalkyl, NR^5, O, SO, SO_2 and S and R^5 and R^6 are independently selected from hydrogen and C_{1-6}alkyl.

[0143] In a further preferred embodiment of the invention X^4 is selected from the group consisting of CH_2, $CHCH_3$, $CH(CH_3)_2$ and NR^5. In a further preferred embodiment of the invention X^4 is NR^5 and R^5 is selected from hydrogen and C_{1-6}alkyl. In a preferred embodiment of the invention R^5 is methyl or hydrogen and R^6 is hydrogen.

[0144] In still a further preferred embodiment of the invention X^4 is O. In yet another preferred embodiment of the invention X^4 is S.

[0145] It is to be understood that the bond between M^2 and X^4 is a single bond in all tautomeric forms.

[0146] Embodiments of the present invention include those wherein Q is a 5- or 6-membered ring.

[0147] When Q is a 5-membered ring, Q is selected from the group consisting of the group consisting of triazolyl, imidazolyl, oxadiazolyl, imidazolonyl, oxazolonyl, thiazolonyl, tetrazolyl and thiadiazolyl, and wherein any substitutable nitrogen atom in the ring is substituted with R^4 on such nitrogen atom.

[0148] In one embodiment the 5 membered ring Q is selected from the group consisting of triazolyl and thiadiazolyl. In another embodiment the 5 membered ring Q is selected from the group consisting of tetrazolyl and oxadiazolyl. In a further embodiment the 5 membered ring Q is imidazolyl.

[0149] When Q is a 6-membered ring, Q is selected from the group consisting of

benzoimidazolyl, benzooxazolyl, tetrahydrotriazolopyridyl, tetrahydrotriazolopyrimidinyl, pyridonyl, pyridazinyl, imidazopyridyl, oxazolopyridyl, thiazolopyridyl, imidazopyridazinyl, oxazolopyridazinyl, thiazolopyridazinyl and purinyl.

[0150] In a preferred embodiment of the invention the 6 membered ring Q is selected from the group consisting of pyridonyl, tetrahydrotriazolopyridyl and tetrahydrotriazolopyrimidinyl. In another embodiment the 6 membered ring Q is pyridazinyl. In a further embodiment the 6 membered ring Q is selected from the group consisting of benzoimidazolyl, benzooxazolyl and imidazopyridyl.

[0151] Q can be further substituted with 0, 1, 2 or 3 substituents R^4, wherein the number of R^4 substituents is designated by the term *m*2. In a preferred embodiment *m2* is 1 or 2. When Q is a 5-membered ring the substituent R^4 is selected from the group consisting of C_{0-6}alkylcyano, $=NC_{1-4}$alkyl, $=NOR^5$, C_{1-4}alkylhalo, halo, C_{1-6}alkyl, OC_{1-4}alkyl, C_{2-4}alkenyl, C_{0-2}alkylC_{3-6}cycloalkyl, C_{0-6}alkylaryl, C_{0-6}alkylheteroaryl, OC_{0-6}alkylaryl, OC_{0-6}alkylheteroaryl, NC_{0-6}alkylaryl, NC_{0-6}alkylheteroaryl, C_{0-6}alkylOaryl, C_{0-6}alkylOheteroaryl, C_{0-6}alkylNaryl, C_{0-6}alkylNheteroaryl, OC_{0-6}alkylOaryl, OC_{0-6}alkylOheteroaryl, OC_{0-6}alkylNaryl, OC_{0-6}alkylNheteroaryl, NC_{0-6}alkylOaryl, NC_{0-6}alkylOheteroaryl, NC_{0-6}alkylNaryl, NC_{0-6}alkylNheteroaryl, $O(CO)C_{1-4}$alkyl, C_{0-4}alkyl$(CO)OC_{1-4}$alkyl, C_{1-4}alkyl$(S)C_{0-4}$alkyl, C_{1-4}alkyl$(SO)C_{0-4}$alkyl, C_{1-4}alkyl$(SO_2)C_{0-4}$alkyl, $(SO)C_{0-4}$alkyl, $(SO_2)C_{0-4}$alkyl, C_{1-4}alkylOR^5, C_{0-4}alkyl$N(C_{1-4}alkyl)_2$ and a 3- or 6-membered non-aromatic ring containing one or more atoms independently selected from C, N, O and S, which ring may optionally be fused with a 5-membered ring containing one or more atoms independently selected from the group consisting of C, N and O and wherein said ring and said fused ring may be substituted by one or two A.

[0152] In a further embodiment of the invention R^4 on the 5 membered Q ring is selected from the group consisting of C_{1-4}alkylhalo, C_{1-6}alkyl, C_{2-4}alkenyl, C_{0-2}alkylC_{3-6}cycloalkyl, C_{0-6}alkylaryl, C_{0-6}alkylheteroaryl, OC_{0-6}alkylaryl, OC_{0-6}alkylheteroaryl, NC_{0-6}alkylaryl, NC_{0-6}alkylheteroaryl, C_{0-6}alkylOaryl, C_{0-6}alkylOheteroaryl, C_{0-6}alkylNaryl, C_{0-6}alkylNheteroaryl, OC_{0-6}alkylOaryl, OC_{0-6}alkylOheteroaryl, OC_{0-6}alkylNaryl, OC_{0-6}alkylNheteroaryl, NC_{0-6}alkylOaryl, NC_{0-}

$_6$alkylOheteroaryl, NC$_{0-6}$alkylNaryl, NC$_{0-6}$alkylNheteroaryl, C$_{0-4}$alkyl(CO)OC$_{1-4}$alkyl, C$_{1-4}$alkyl(S)C$_{0-4}$alkyl, C$_{1-4}$alkylOR^5 and a 3- or 6-membered non-aromatic ring containing one or more atoms independently selected from C, N, O and S, which ring may optionally be fused with a 5-membered ring containing one or more atoms independently selected from the group consisting of C, N and O and wherein said ring and said fused ring may be substituted by one or two A.

[0153] In one embodiment of the invention Q is selected from the group consisting of triazolyl, imidazolyl, oxadiazolyl, imidazolonyl, oxazolonyl, thiazolonyl, tetrazolyl and thiadiazolyl, and wherein any substitutable nitrogen atom in the ring is substituted with R^4 on such nitrogen atom and R^4 is selected from the group consisting of C$_{1-4}$alkylhalo, C$_{1-6}$alkyl, C$_{2-4}$alkenyl, C$_{0-2}$alkylC$_{3-6}$cycloalkyl, C$_{0-6}$alkylaryl, C$_{0-6}$alkylheteroaryl, OC$_{0-6}$alkylaryl, OC$_{0-6}$alkylheteroaryl, NC$_{0-6}$alkylaryl, NC$_{0-6}$alkylheteroaryl,C$_{0-6}$alkylOaryl, C$_{0-6}$alkylOheteroaryl, C$_{0-6}$alkylNaryl, C$_{0-6}$alkylNheteroaryl, OC$_{0-6}$alkylOaryl, OC$_{0-6}$alkylOheteroaryl, OC$_{0-6}$alkylNaryl, OC$_{0-6}$alkylNheteroaryl, NC$_{0-6}$alkylOaryl, NC$_{0-6}$alkylOheteroaryl, NC$_{0-6}$alkylNaryl, NC$_{0-6}$alkylNheteroaryl, C$_{0-4}$alkyl(CO)OC$_{1-4}$alkyl, C$_{1-4}$alkyl(S)C$_{0-4}$alkyl, C$_{1-4}$alkylOR^5 and a 3- or 6-membered non-aromatic ring containing one or more atoms independently selected from C, N, O and S, which ring may optionally be fused with a 5-membered ring containing one or more atoms independently selected from the group consisting of C, N and O and wherein said ring and said fused ring may be substituted by one or two A.

[0154] In another embodiment of the invention Q selected from the group consisting of triazolyl, imidazolyl, oxadiazolyl, tetrazolyl and thiadiazolyl, and wherein any substitutable nitrogen atom in the ring is substituted with R^4 on such nitrogen atom and R^4 is selected from the group consisting of C$_{1-4}$alkylhalo, C$_{1-6}$alkyl, C$_{2-4}$alkenyl, C$_{0-2}$alkylC$_{3-6}$cycloalkyl, C$_{0-6}$alkylaryl, C$_{0-6}$alkylheteroaryl, OC$_{0-6}$alkylaryl, OC$_{0-6}$alkylheteroaryl, NC$_{0-6}$alkylaryl, NC$_{0-6}$alkylheteroaryl,C$_{0-6}$alkylOaryl, C$_{0-6}$alkylOheteroaryl, C$_{0-6}$alkylNaryl, C$_{0-6}$alkylNheteroaryl, OC$_{0-6}$alkylOaryl, OC$_{0-6}$alkylOheteroaryl, OC$_{0-6}$alkylNaryl, OC$_{0-6}$alkylNheteroaryl, NC$_{0-6}$alkylOaryl, NC$_{0-6}$alkylOheteroaryl, NC$_{0-6}$alkylNaryl, NC$_{0-6}$alkylNheteroaryl, C$_{0-4}$alkyl(CO)OC$_{1-4}$alkyl, C$_{1-4}$alkyl(S)C$_{0-4}$alkyl, C$_{1-4}$alkylOR^5 and a 3- or 6-membered non-aromatic ring

containing one or more atoms independently selected from C, N, O and S, which ring may optionally be fused with a 5-membered ring containing one or more atoms independently selected from the group consisting of C, N and O and wherein said ring and said fused ring may be substituted by one or two A.

[0155] When Q is a 6-membered ring the substituent R^4 is selected from the group consisting of hydrogen, hydroxy, C_{0-6}alkylcyano, $=NR^5$, $=NOR^5$, C_{1-4}alkylhalo, halo, C_{1-6}alkyl, OC_{1-4}alkyl, OC_{0-6}alkylaryl, $O(CO)C_{1-4}$alkyl, C_{0-4}alkyl(S)C_{0-4}alkyl, C_{1-4}alkyl(SO)C_{0-4}alkyl, C_{1-4}alkyl(SO_2)C_{0-4}alkyl, (SO)C_{0-4}alkyl, (SO_2)C_{0-4}alkyl, C_{1-4}alkylOR^5, C_{0-4}alkylNR^5R^6 and a 5- or 6-membered ring containing one or more atoms independently selected from C, N, O and S, which ring may optionally be fused with a 5- or 6-membered ring containing one or more atoms independently selected from the group consisting of C, N and O and wherein said ring and said fused ring may be substituted by one or two A.

[0156] In a suitable embodiment of the invention R^4 on the 6 membered Q ring is selected from hydrogen and C_{1-6}alkyl. In a further embodiment of the invention R^4 is hydrogen, methyl, ethyl, propyl, butyl or hexyl.

[0157] In a preferred embodiment of the invention Q selected from the group consisting of benzoimidazolyl, benzooxazolyl, tetrahydrotriazolopyridyl, tetrahydrotriazolopyrimidinyl, pyridonyl, pyridazinyl, imidazopyridyl, oxazolopyridyl, thiazolopyridyl, imidazopyridazinyl, oxazolopyridazinyl, thiazolopyridazinyl and purinyl and R^4 is hydrogen or C_{1-6}alkyl.

[0158] In another preferred embodiment of the invention Q selected from the group consisting of benzoimidazolyl, benzooxazolyl, tetrahydrotriazolopyridyl, tetrahydrotriazolopyrimidinyl, pyridonyl, pyridazinyl and imidazopyridyl, and R^4 is hydrogen or C_{1-6}alkyl.

[0159] In a suitable embodiment of the invention R^4 is selected from the group consisting of benzo[b]thiophenyl, benzodioxolyl, bromo, bromofuryl, butoxyphenyl, chloromethoxypyridyl, chlorophenyl, chlorophenylmethanol, chloropyridyl, chlorothiophene, cyanophenyl, cyclohexyl, cyclopentyl, dichloro-phenyl, dichloropyridyl, difluorophenyl, dimethylthiazolyl, ethanol, ethoxymethyl, fluoromethylphenyl, fluorophenyl, formic acid methyl ester, furyl, hydrogen,

hydroxyphenoxymethyl, hydroxyphenyl, imidazolyl, methoxyethyl, methoxymethyl, methoxyphenoxymethyl, methoxyphenyl, methoxyphenylethyl, methoxypyridazinyl, methoxypyridyl, methoxypyrimidinyl, methoxythiophene, methylimidazolyl, methylpyridyl, methylsulfanylmethyl, methylthiazolyl, methylthiophene, nitrofuryl, nitrophenyl, phenyl, p-tolyloxymethyl, pyridazinyl, pyridine-oxidyl, benzylmorpholinyl, pyridinolyl, pyridyl, pyridylmethyl, pyrimidinyl, tert-butylphenyl, tetrahydrofuryl, thiazolyl, thiophene, tolyl, trifluoromethyl, acetic acid methylester, allyl, amino, benzyl, cyclopropylmethyl, ethyl, fluorobenzyl, fluoroethyl, furylmethyl, hydroxyethyl, isobutyl, methyl, methylbenzyl, methylbutyl, methylsulfanylpropyl, *n*-butyl, *n*-hexyl, *n*-propyl, tetrahydrofurylmethyl, thiophenylmethyl and trifluoroethyl.

[0160] Ring Q may be substituted by one or more R^4 on a carbon and/or a nitrogen atom in the ring. When Q is substituted on the carbon atom, R^4 is selected from benzo[b]thiophenyl, benzodioxolyl, bromo, bromofuryl, butoxyphenyl, chloromethoxypyridyl, chlorophenyl, chlorophenylmethanol, chloropyridyl, chlorothiophene, cyanophenyl, cyclohexyl, cyclopentyl, dichloro-phenyl, dichloropyridyl, difluorophenyl, dimethylthiazolyl, ethanol, ethoxymethyl, fluoromethylphenyl, fluorophenyl, formic acid methyl ester, furyl, hydrogen, hydroxyphenoxymethyl, hydroxyphenyl, imidazolyl, methoxyethyl, methoxymethyl, methoxyphenoxymethyl, methoxyphenyl, methoxyphenylethyl, methoxypyridazinyl, methoxypyridyl, methoxypyrimidinyl, methoxythiophene, methylimidazolyl, methylpyridyl, methylsulfanylmethyl, methylthiazolyl, methylthiophene, nitrofuryl, nitrophenyl, phenyl, p-tolyloxymethyl, pyridazinyl, pyridine-oxidyl, benzylmorpholinyl, pyridinolyl, pyridyl, pyridylmethyl, pyrimidinyl, tert-butylphenyl, tetrahydrofuryl, thiazolyl, thiophene, tolyl and trifluoromethyl.

[0161] When Q is substituted on the nitrogen atom, R^4 is selected from acetic acid methylester, allyl, amino, benzyl, cyclopropyl, cyclopropylmethyl, ethyl, flourobenzyl, fluoroethyl, furylmethyl, hydroxyethyl, isobutyl, methoxyethyl, methyl, methylbenzyl, methylbutyl, methylsulfanylpropyl, *n*-butyl, *n*-hexyl, *n*-propyl, tetrahydrofurylmethyl, thiophenylmethyl and trifluoroethyl.

[0162] When R^4 is a ring R^4 can be substituted with one or more substituents A, wherein A is selected from hydrogen, hydroxy, halo, nitro, oxo, $C_{0\text{-}6}$alkylcyano, $C_{0\text{-}}$

$_4$alkylC$_{3-6}$cycloalkyl, C$_{1-6}$alkyl, C$_{1-6}$alkylhalo, OC$_{1-6}$alkylhalo, C$_{2-6}$alkenyl, C$_{0-3}$alkylaryl, C$_{0-6}$alkylOR^5, OC$_{2-6}$alkylOR^5, C$_{1-6}$alkylSR^5, OC$_{2-6}$alkylSR^5, (CO)R^5, O(CO)R^5, OC$_{2-6}$alkylcyano, OC$_{1-6}$alkylCO$_2$R^5, O(CO)OR^5, OC$_{1-6}$alkyl(CO)R^5, C$_{1-6}$alkyl(CO)R^5, NR^{5}OR^6, OC$_{2-6}$alkylNR^{5}R^6, C$_{0-6}$alkyl(CO)NR^{5}R^6, OC$_{1-6}$alkyl(CO)NR^{5}R^6, OC$_{2-6}$alkylNR^5(CO)R^6, C$_{0-6}$alkylNR^5(CO)R^6, C$_{0-6}$alkylNR^5(CO)NR^{5}R^6, O(CO)NR^{5}R^6, C$_{0-6}$alkyl(SO$_2$)NR^{5}R^6, OC$_{2-6}$alkyl(SO$_2$)NR^{5}R^6, C$_{0-6}$alkylNR^5(SO$_2$)R^6, OC$_{2-6}$alkylNR^5(SO$_2$)R^6, SO$_3$R^5, C$_{1-6}$alkylNR^5(SO$_2$)NR^{5}R^6, OC$_{2-6}$alkyl(SO$_2$)R^5, C$_{0-6}$alkyl(SO$_2$)R^5, C$_{0-6}$alkyl(SO)R^5, OC$_{2-6}$alkyl(SO)R^5 and a 5-membered ring containing one or more atoms independently selected from the group consisting of C, N, O and S.

[0163] In a preferred embodiment A is selected from hydroxy, halo, nitro, oxo, C$_{0-6}$alkylcyano, C$_{1-6}$alkyl, C$_{2-6}$alkenyl, C$_{0-3}$alkylaryl, C$_{0-6}$alkylOR^5 and a 5-membered ring containing one or more atoms independently selected from the group consisting of C and O.

[0164] Specific embodiments of the invention include,

2-[5-(3-Methoxy-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1*H*-benzoimidazole,

5-(3-Methoxy-phenyl)-3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-[5-(1-Methyl-5-thiophen-2-yl-1*H*-imidazol-2-ylsulfanylmethyl)-[1,2,4]oxadiazol-3-yl]-benzonitrile,

3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]traiazol-3-ylsulfanylmethyl)-5-phenyl-[1,2,4]oxadiazole,

2-[5-(3-Methoxy-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-5-methyl-1*H*-benzoimidazole,

3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-trifluoromethyl-phenyl)-[1,2,4]oxadiazole,

3-(3-Methoxy-phenyl)-5-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-3-phenyl-[1,2,4]oxadiazole,

5-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-3-m-tolyl-[1,2,4]oxadiazole,

3-[3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzonitrile,

3-[4-Methyl-5-(2-methyl-thiazol-4-yl)-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl]-5-m-tolyl-[1,2,4]oxadiazole,

3-[5-(2-Methyl-thiazol-4-yl)-[1,3,4]oxadiazol-2-ylsulfanylmethyl]-5-m-tolyl-[1,2,4]oxadiazole,

3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-2-yl-[1,2,4]oxadiazole,

3-[5-(2,4-Dimethyl-thiazol-5-yl)-4-methyl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl]-5-m-tolyl-[1,2,4]oxadiazole,

3-[4-Methyl-5-(5-nitro-furan-2-yl)-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl]-5-m-tolyl-[1,2,4]oxadiazole,

4-[4-Methyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4*H*-[1,2,4]triazol-3-yl]-pyridine,

3-[5-(4-tert-Butyl-phenyl)-4-methyl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl]-5-m-tolyl-[1,2,4]-oxadiazole,

2-Chloro-5-[4-methyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4*H*-[1,2,4]triazol-3-yl]-pyridine,

2-[5-(3-Methoxy-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-benzooxazole,

3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-3-yl-[1,2,4]oxadiazole,

3-(5-Furan-2-yl-4-methyl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

5-(3-Fluoro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

2-(5-m-Tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-pyridine,

2-[5-(3-Methoxy-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1*H*-imidazo[4,5-

b]pyridine,

5-(3-Fluoro-5-methyl-phenyl)-3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-Methyl-5-[3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine,

3-(4-Methyl-5-phenyl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

2-[4-Methyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4*H*-[1,2,4]triazol-3-yl]-pyridine,

4-Benzyl-2-[4-methyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4*H*-[1,2,4]triazol-3-yl]-morpholine,

4-[4-Methyl-5-(5-thiophen-3-yl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4*H*-[1,2,4]triazol-3-yl]-pyridine,

3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiazol-4-yl-[1,2,4]oxadiazole,

3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-nitro-phenyl)-[1,2,4]oxadiazole,

2-Methyl-4-[3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine,

3-[4-Methyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4*H*-[1,2,4]triazol-3-yl]-pyridine,

3-(4-Methyl-5-thiophene-3-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

3-(4-Methyl-5-thiazol-4-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

5-(3-Iodo-phenyl)-3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Ethyl-phenyl)-3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

2-[5-(2-Methyl-pyridin-4-yl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1*H*-benzoimidazole,

2-[5-(3-Iodo-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1*H*-benzoimidazole,

3-(4-Methyl-5-trifluoromethyl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

2,6-Dichloro-4-[4-methyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4*H*-[1,2,4]triazol-3-yl]-pyridine,

3-(4-Methyl-5-p-tolyl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

Dimethyl-{3-[3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]phenyl}-amine,

5-(3-Chloro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-trifluoromethoxy-phenyl)[1,2,4]oxadiazole,

3-(5-Cyclohexyl-4-methyl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

3-(5-tert-Butyl-4-methyl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

5-(3-Bromo-phenyl)-3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

2-[5-(3-Bromo-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1*H*-benzoimidazole,

5-(3-Methoxymethyl-phenyl)-3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-lsulfanylmethyl)-[1,2,4]oxadiazole,

2-[5-(3-Methoxymethyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1*H*-benzoimidazole,

4-[5-(4-Methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-3-yl]-pyridine,

2-{1-[5-(3-Methoxy-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-1-methyl-1*H*-imidazo[4,5-b]pyridine,

2-[5-(3-Methoxy-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1-methyl-1*H*-imidazo[4,5-b],

3-[1-Methyl-1-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-5-

m-tolyl-[1,2,4]oxadiazole,

3-[1-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-5-m-tolyl-[1,2,4]oxadiazole,

3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazole-3-sulfonylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazole-3-sulfinylmethyl)-5-m-tolyl-[1,2,4]oxadiazole, or

5-(3-Furan-3-yl-phenyl)-3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

or salt thereof.

[0165] Further specific embodiments of the invention include,

4-(4-Cyclopropyl-5-{1-[5-(2,5-difluoro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[5-(3-Methoxy-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-{4-Methyl-5-[1-(5-m-tolyl-[1,2,4]oxadiazol-3-yl)-ethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

5-(4-Methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-o-tolyl-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(4-cyclopropyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

2-{3-[5-(2-Fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-5-thiophen-2-yl-[1,2,4]triazol-4-yl}-ethanol,

4-{4-Ethyl-5-[5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyrimidine,

3-(4-Ethyl-5-furan-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazole,

{3-[5-(2-Fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-5-thiophen-2-yl-[1,2,4]triazol-4-yl}-acetic acid methyl ester,

5-(2-Fluoro-5-methyl-phenyl)-3-[5-furan-2-yl-4-(2-methoxy-ethyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

3-(4-Cyclopropyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazole,

3-(5-Chloro-2-fluoro-phenyl)-5-(4-cyclopropylmethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-{5-[3-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyrimidine,

3-(5-Cyclopentyl-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

3-(3-Chloro-phenyl)-5-{4-ethyl-5-[2-(4-methoxy-phenyl)-ethyl]-4H-[1,2,4]triazol-3-ylsulfanylmethyl}-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(4-ethyl-5-p-tolyloxymethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-(2-methoxy-ethyl)-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

3-(5-Chloro-2-fluoro-phenyl)-5-(4-ethyl-5-methoxymethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(5-Chloro-2-fluoro-phenyl)-3-(4-ethyl-5-methoxymethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(4-ethyl-5-methoxymethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-(3-Chloro-phenyl)-5-(4-ethyl-5-methoxymethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-(5-{1-[3-(3-Chloro-phenyl)-isoxazol-5-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

3-(4-Allyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-chloro-phenyl)-[1,2,4]oxadiazole,

3-(4-Allyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-3-yl-[1,2,4]oxadiazole,

5-(4-Allyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-furan-2-yl-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-ethyl-5-(4-methoxy-phenoxymethyl)-4H-[1,2,4]triazol-

3-ylsulfanylmethyl]-[1,2,4]oxadiazole,
3-(3-Chloro-phenyl)-5-[4-ethyl-5-(4-methoxy-phenoxymethyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,
{5-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-methanol,
3-(3-Chloro-phenyl)-5-[4-ethyl-5-(2-methoxy-ethyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,
3-(3-Chloro-phenyl)-5-(4-ethyl-5-methylsulfanylmethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,
3-(3-Chloro-phenyl)-5-(5-ethoxymethyl-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,
5-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazole-3-carboxylic acid methyl ester,
2-(5-Chloro-2-fluoro-phenyl)-5-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazole,
2-(3-Chloro-phenyl)-5-(4-cyclopropyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazole,
5-(3-Chloro-phenyl)-3-{1-[4-ethyl-5-(tetrahydro-furan-2-yl)-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,2,4]oxadiazole,
4-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyridazine,
4-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-ylmethyl)-pyridine,
5-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyridin-2-ol,
4-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-phenol,
5-(3-Chloro-phenyl)-3-[5-(4-methoxy-phenoxymethyl)-4-(tetrahydro-furan-2-ylmethyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,
5-(3-Chloro-phenyl)-3-[4-cyclopropyl-5-(4-methoxy-phenoxymethyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(5-Chloro-2-fluoro-phenyl)-3-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-(4-Ethyl-5-methoxymethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

3-[4-Ethyl-5-(tetrahydro-furan-2-yl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-5-m-tolyl-[1,2,4]oxadiazole,

2-(3-Chloro-phenyl)-5-{1-[4-ethyl-5-(4-methoxy-phenyl)-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,3,4]oxadiazole,

4-{5-[3-(2,5-Difluoro-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyrimidine,

4-{5-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyrimidine,

3-(3-Chloro-phenyl)-5-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Methylsulfanyl-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

2-[5-(3-Methylsulfanyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1H-benzoimidazole,

5-(2,5-Dimethyl-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(2-Fluoro-5-methyl-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Cyclopropyl-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-{5-[2-(3-Chloro-phenyl)-oxazol-4-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-[4-Methyl-5-(5-thiophen-2-yl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine,

4-{4-Methyl-5-[5-(3-methylsulfanyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-

[1,2,4]triazol-3-yl}-pyridine,

2-Methyl-4-[3-(4-methyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine,

1-{3-[3-(4-Methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-phenyl}-ethanone,

4-{5-[5-(2-Fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

2-Methyl-4-[4-methyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine,

3-[5-(3-Chloro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazole,

4-{5-[5-(3-Chloro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

3-(4-Butyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-chloro-phenyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-(3-methoxy-propyl)-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

3-(4-Benzyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-chloro-phenyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(4-furan-2-ylmethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

5-(3-Chloro-phenyl)-3-(4-methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-2-methyl-pyridine,

5-(5-Chloro-2-fluoro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-{5-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

3-{5-[5-(2-Fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

5-(3-Chloro-phenyl)-3-(5-thiophen-2-yl-4-thiophen-2-ylmethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-{5-[3-(2-Fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{5-[3-(2-Fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{5-[5-(5-Bromo-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

3-{5-[5-(5-Bromo-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

5-(5-Bromo-2-fluoro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(4-Methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-phenyl-[1,2,4]oxadiazole,

3-{5-[5-(3-Fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{5-[5-(3-Fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

5-(3-Fluoro-phenyl)-3-(4-methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-[4-Methyl-5-(5-thiophen-3-yl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine,

3-(4-Methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-3-yl-[1,2,4]oxadiazole,

2-Chloro-4-[3-(4-methyl-5-pyridin-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine,

2-Chloro-4-[3-(4-methyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-

[1,2,4]oxadiazol-5-yl]-pyridine,

2-Chloro-4-[3-(4-methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine,

4-[4-Methyl-5-(5-phenyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine,

3-(4-Methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-phenyl-[1,2,4]oxadiazole,

5-(5-Bromo-2-fluoro-phenyl)-3-(4-methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-[5-(3-Chloro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazole,

2-Chloro-4-[3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine,

4-{5-[3-(3-Fluoro-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

3-(3-Fluoro-phenyl)-5-(4-methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazole,

4-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-furan-2-ylmethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

3-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

5-(3-Chloro-phenyl)-3-(4-ethyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-furan-2-ylmethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

3-(4-Furan-2-ylmethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

5-(5-Fluoro-2-methyl-phenyl)-3-(4-furan-2-ylmethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(4-furan-2-ylmethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-[3-(4-Methyl-5-pyridin-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzonitrile,

3-[3-(4-Methyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzonitrile,

3-[3-(4-Methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzonitrile,

5-(5-Chloro-2-fluoro-phenyl)-3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

2-Chloro-4-[3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine,

3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-3-yl-[1,2,4]oxadiazole,

3-(4-Ethyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

4-[4-Ethyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine,

3-[4-Ethyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine,

3-(4-Ethyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazole,

4-{4-Ethyl-5-[5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

3-{4-Ethyl-5-[5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

3-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-5-pyridin-4-yl-

[1,2,4]triazol-4-ylamine,

4-{5-[5-(5-Bromo-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

5-(4-Methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-thiophen-2-yl-[1,2,4]oxadiazole,

3-[3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzonitrile,

3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-phenyl-[1,2,4]oxadiazole,

4-[3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-2-methoxy-pyridine,

3-(3-Chloro-phenyl)-5-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-{5-[5-(3-Chloro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

2-Methyl-4-[3-(4-methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine,

4-[3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-2-methyl-pyridine,

5-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-thiophen-2-yl-[1,2,4]oxadiazole,

4-{5-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-[3-(4-Ethyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-2-methyl-pyridine,

3-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-benzonitrile,

5-(3-Chloro-phenyl)-3-[5-(3-chloro-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[5-(4-chloro-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

4-{5-[5-(2,5-Dichloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

5-(2,5-Dichloro-phenyl)-3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(2,5-Difluoro-phenyl)-3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-{5-[5-(2,5-Difluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

5-(2,5-Dichloro-phenyl)-3-(4-ethyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(2,5-Difluoro-phenyl)-3-(4-ethyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-propyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{5-[5-(2-Fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-propyl-4H-[1,2,4]triazol-3-yl}-pyridine,

3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-2-yl-[1,2,4]oxadiazole,

3-(4-Methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-2-yl-[1,2,4]oxadiazole,

4-[4-Methyl-5-(3-thiophen-3-yl-[1,2,4]oxadiazol-5-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine,

5-(4-Methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-thiophen-3-yl-[1,2,4]oxadiazole,

5-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-thiophen-3-yl-[1,2,4]oxadiazole,

5-[3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-thiophene-3-carbonitrile,

5-(3-Chloro-phenyl)-3-[5-(2-fluoro-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[5-(3-fluoro-phenyl)-4-methyl-4H-[1,2,4]triazol-3-

ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[5-(4-fluoro-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

3-(5-Benzo[b]thiophen-2-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-chloro-phenyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[5-(3-methoxy-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[5-(4-methoxy-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

3-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazole,

3-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole,

3-(4-Ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazole,

3-[5-(2-Fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-5-pyridin-4-yl-[1,2,4]triazol-4-ylamine,

3-[5-(2-Fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-5-thiophen-2-yl-[1,2,4]triazol-4-ylamine,

3-Pyridin-4-yl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-[1,2,4]triazol-4-ylamine,

3-Thiophen-2-yl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-[1,2,4]triazol-4-ylamine,

3-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-3-yl-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-[3-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-2-methyl-pyridine,

5-(2,5-Difluoro-phenyl)-3-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-[4-Ethyl-5-(5-thiophen-3-yl-isoxazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine,

4-Ethyl-3-furan-2-yl-5-(5-thiophen-3-yl-isoxazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazole,

5-(3-Chloro-phenyl)-3-[5-(3,5-dichloro-phenyl)-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(4-ethyl-5-p-tolyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(4-ethyl-5-m-tolyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-ethyl-5-(3-nitro-phenyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

4-{5-[3-(3-Chloro-phenyl)-isoxazol-5-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

5-(3-Chloro-phenyl)-3-[5-(2,5-difluoro-phenyl)-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[5-(3-chloro-phenyl)-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[5-(4-chloro-phenyl)-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

4-{5-[5-(3-Chloro-phenyl)-oxazol-2-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

3-[5-(3-Chloro-phenyl)-oxazol-2-ylmethylsulfanyl]-4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazole,

3-[5-(3-Chloro-phenyl)-oxazol-2-ylmethylsulfanyl]-4-ethyl-5-furan-2-yl-4H-[1,2,4]triazole,

5-(2-Chloro-5-methyl-phenyl)-3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-{5-[3-(3-Chloro-phenyl)-isoxazol-5-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

3-[3-(3-Chloro-phenyl)-isoxazol-5-ylmethylsulfanyl]-4-ethyl-5-thiophen-2-yl-4H-

[1,2,4]triazole,

3-[3-(3-Chloro-phenyl)-isoxazol-5-ylmethylsulfanyl]-4-ethyl-5-furan-2-yl-4H-[1,2,4]triazole,

4-{5-[5-(2-Fluoro-5-methyl-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

5-(2,5-Dichloro-thiophen-3-yl)-3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-{5-[5-(2,5-Dichloro-thiophen-3-yl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{4-Ethyl-5-[5-(2-fluoro-5-methyl-phenyl)-isoxazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

4-Ethyl-3-[5-(2-fluoro-5-methyl-phenyl)-isoxazol-3-ylmethylsulfanyl]-5-thiophen-2-yl-4H-[1,2,4]triazole,

4-Ethyl-3-[5-(2-fluoro-5-methyl-phenyl)-isoxazol-3-ylmethylsulfanyl]-5-furan-2-yl-4H-[1,2,4]triazole,

5-(3-Chloro-phenyl)-3-(4-ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-(3-Chloro-phenyl)-5-(4-ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-(4-Ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-3-yl-[1,2,4]oxadiazole,

5-(4-Ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-thiophen-3-yl-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-ethyl-5-(3-fluoro-phenyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-ethyl-5-(4-fluoro-phenyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

3-(4-Ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-2-yl-[1,2,4]oxadiazole,

3-{3-[5-(3-Chloro-thiophen-2-yl)-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazol-5-yl}-benzonitrile,

4-{5-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

2-(3-Chloro-phenyl)-5-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-ethyl-5-(4-methoxy-phenyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[5-(2-fluoro-5-methyl-phenyl)-4-furan-2-ylmethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

4-[3-(4-Ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-2-methyl-pyridine,

3-(4-Ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-methoxy-phenyl)-[1,2,4]oxadiazole,

5-(4-Ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-(3-methoxy-phenyl)-[1,2,4]oxadiazole,

5-(4-Ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-thiophen-2-yl-[1,2,4]oxadiazole,

5-(5-Chloro-2-fluoro-phenyl)-3-(4-ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-[3-(4-Ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzonitrile,

3-[5-(3-Chloro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-ethyl-5-trifluoromethyl-4H-[1,2,4]triazole,

3-[5-(3-Chloro-phenyl)-oxazol-2-ylmethylsulfanyl]-4-ethyl-5-trifluoromethyl-4H-[1,2,4]triazole,

4-Ethyl-3-(5-thiophen-3-yl-isoxazol-3-ylmethylsulfanyl)-5-trifluoromethyl-4H-[1,2,4]triazole,

4-{3-[5-(3-Fluoro-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazol-5-yl}-2-methyl-pyridine,

4-{3-[5-(3-Chloro-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazol-5-yl}-2-methyl-pyridine,

4-{3-[5-(4-Chloro-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-

[1,2,4]oxadiazol-5-yl}-2-methyl-pyridine,

4-{3-[5-(4-Methoxy-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazol-5-yl}-2-methyl-pyridine,

4-[3-(4-Ethyl-5-p-tolyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-2-methyl-pyridine,

3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-fluoro-phenyl)-[1,2,4]oxadiazole,

4-{4-Ethyl-5-[5-(3-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

5-(3-Chloro-phenyl)-3-[5-(3,5-difluoro-phenyl)-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[5-(2,6-difluoro-phenyl)-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

2-[3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-4-methyl-phenol,

3-{1-[5-(3-Chloro-phenyl)-isoxazol-3-yl]-ethylsulfanyl}-4-ethyl-5-furan-2-yl-4H-[1,2,4]triazole,

4-(5-{1-[5-(3-Chloro-phenyl)-isoxazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyridine,

3-[5-(4-Butoxy-phenyl)-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-5-(3-chloro-phenyl)-[1,2,4]oxadiazole,

3-(5-Benzo[1,3]dioxol-5-yl-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-chloro-phenyl)-[1,2,4]oxadiazole,

3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(2-methyl-thiazol-4-yl)-[1,2,4]oxadiazole,

3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(4-fluoro-phenyl)-[1,2,4]oxadiazole,

4-Ethyl-3-{1-[5-(2-fluoro-5-methyl-phenyl)-isoxazol-3-yl]-ethylsulfanyl}-5-furan-2-yl-4H-[1,2,4]triazole,

4-(4-Ethyl-5-{1-[5-(2-fluoro-5-methyl-phenyl)-isoxazol-3-yl]-ethylsulfanyl}-4H-[1,2,4]triazol-3-yl)-pyridine,

5-(3-Chloro-phenyl)-3-[4-ethyl-5-(3-methyl-3H-imidazol-4-yl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-ethyl-5-(1-methyl-1H-imidazol-2-yl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-ethyl-5-(1-methyl-1H-imidazol-4-yl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

4-{5-[5-(3-Chloro-phenyl)-4-methyl-isoxazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

3-[5-(3-Chloro-phenyl)-4-methyl-isoxazol-3-ylmethylsulfanyl]-4-ethyl-5-furan-2-yl-4H-[1,2,4]triazole,

3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(4-methyl-thiophen-2-yl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-ethyl-5-(3-methyl-thiophen-2-yl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-ethyl-5-(5-methyl-thiophen-2-yl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

4-{5-[4-Chloro-5-(3-chloro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

3-[4-Chloro-5-(3-chloro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-ethyl-5-furan-2-yl-4H-[1,2,4]triazole,

2-Chloro-4-{5-[5-(3-chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-6-methyl-pyridine,

3-[5-(5-Bromo-furan-2-yl)-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-5-(3-chloro-phenyl)-[1,2,4]oxadiazole,

2-Chloro-4-{5-[5-(3-chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

2-Chloro-4-{5-[5-(3-chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-6-methoxy-pyridine,

2-[3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-4-methyl-benzonitrile,

5-(3-Chloro-phenyl)-3-[4-ethyl-5-(3-methoxy-thiophen-2-yl)-4H-[1,2,4]triazol-3-

ylsulfanylmethyl]-[1,2,4]oxadiazole,

3-[5-(5-Chloro-thiophen-3-yl)-isoxazol-3-ylmethylsulfanyl]-4-ethyl-5-furan-2-yl-4H-[1,2,4]triazole,

3-[3-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-5-fluoro-benzonitrile,

4-Ethyl-3-(5-phenyl-isoxazol-3-ylmethylsulfanyl)-5-thiophen-2-yl-4H-[1,2,4]triazole,

4-Methyl-3-(5-phenyl-isoxazol-3-ylmethylsulfanyl)-5-thiophen-3-yl-4H-[1,2,4]triazole,

4-Ethyl-3-furan-2-yl-5-(5-phenyl-isoxazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazole,

4-[4-Ethyl-5-(5-phenyl-isoxazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine,

4-[4-Methyl-5-(5-phenyl-isoxazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine,

2-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,3,4]oxadiazole,

4-[4-Methyl-5-(5-m-tolyl-[1,3,4]oxadiazol-2-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine,

4-[4-Ethyl-5-(5-m-tolyl-[1,3,4]oxadiazol-2-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine,

4-{5-[5-(5-Chloro-thiophen-3-yl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

3-[3-(4-Ethyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-4-fluoro-benzonitrile,

3-[3-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-4-fluoro-benzonitrile,

3-[3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-4-fluoro-benzonitrile,

3-[3-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzonitrile,

3-[5-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-

[1,2,4]oxadiazol-3-yl]-benzonitrile,

3-[3-(4-Methyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzonitrile,

5-(5-Chloro-2-fluoro-phenyl)-3-(4-methyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

2-Chloro-4-[3-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine,

2-Chloro-4-[3-(5-furan-2-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine,

2-(3-Chloro-phenyl)-5-[4-methyl-5-(2-methyl-thiazol-4-yl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,3,4]oxadiazole,

2-(3-Chloro-phenyl)-5-(4-methyl-5-thiazol-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazole,

2-(3-Chloro-phenyl)-5-(5-furan-2-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazole,

2-(3-Chloro-phenyl)-5-(4-ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazole,

4-{4-Ethyl-5-[5-(4-methyl-thiophen-2-yl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

3-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(4-methyl-thiophen-2-yl)-[1,2,4]oxadiazole,

3-(3-Chloro-phenyl)-5-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-{5-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{4-Ethyl-5-[5-(3-nitro-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

2-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-nitro-phenyl)-[1,3,4]oxadiazole,

4-{5-[5-(3-Chloro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-cyclopropyl-4H-[1,2,4]triazol-3-yl}-pyridine,

3-[5-(3-Chloro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-ethyl-5-(4-methoxy-phenyl)-4H-[1,2,4]triazole,

5-(3-Chloro-phenyl)-3-[1-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[1-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,2,4]oxadiazole,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyridine,

3-[5-(4-Ethyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-benzonitrile,

3-[5-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-benzonitrile,

3-[5-(4-Methyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-benzonitrile,

3-[5-(4-Cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-benzonitrile,

4-{5-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{5-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4-cyclopropyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{5-[5-(5-Chloro-2-fluoro-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4-cyclopropyl-4H-[1,2,4]triazol-3-yl}-pyridine,

2-(5-Chloro-2-fluoro-phenyl)-5-[4-ethyl-5-(4-methoxy-phenyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,3,4]oxadiazole,

4-{5-[5-(5-Chloro-2-fluoro-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{5-[5-(5-Chloro-2-fluoro-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

2-(3-Chloro-phenyl)-5-[4-ethyl-5-(4-methoxy-phenyl)-4H-[1,2,4]triazol-3-

ylsulfanylmethyl]-[1,3,4]oxadiazole,

2-(3-Chloro-phenyl)-5-[1-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,3,4]oxadiazole,

5-(5-Chloro-2-fluoro-phenyl)-3-[1-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,2,4]oxadiazole,

4-(5-{1-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyridine,

2-Chloro-4-[3-(4-cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine,

4-{5-[5-(2-Fluoro-5-methyl-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{4-Ethyl-5-[5-(2-fluoro-5-methyl-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{4-Cyclopropyl-5-[5-(2-fluoro-5-methyl-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

2-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(2-fluoro-5-methyl-phenyl)-[1,3,4]oxadiazole,

2-[4-Ethyl-5-(4-methoxy-phenyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-5-(2-fluoro-5-methyl-phenyl)-[1,3,4]oxadiazole,

4-{5-[5-(5-Chloro-2-fluoro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-(5-{1-[5-(5-Chloro-2-fluoro-phenyl)-isoxazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-{5-[5-(5-Chloro-2-fluoro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-(5-{1-[5-(5-Chloro-2-fluoro-phenyl)-isoxazol-3-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-{5-[5-(5-Chloro-2-fluoro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-cyclopropyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-(5-{1-[5-(5-Chloro-2-fluoro-phenyl)-isoxazol-3-yl]-ethylsulfanyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

3-[5-(5-Chloro-2-fluoro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-ethyl-5-furan-2-yl-4H-[1,2,4]triazole,

3-{1-[5-(5-Chloro-2-fluoro-phenyl)-isoxazol-3-yl]-ethylsulfanyl}-4-ethyl-5-furan-2-yl-4H-[1,2,4]triazole,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

5-(5-Chloro-2-fluoro-phenyl)-3-(5-furan-2-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(5-Chloro-2-fluoro-phenyl)-3-(5-furan-3-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-Chloro-2-[3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-phenol,

2-Chloro-4-[5-(4-methyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-pyridine,

2-Chloro-4-[5-(4-ethyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-pyridine,

2-Chloro-4-[5-(4-cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-pyridine,

2-Chloro-4-[5-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-pyridine,

2-Chloro-4-{5-[4-ethyl-5-(4-methoxy-phenyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,3,4]oxadiazol-2-yl}-pyridine,

2-(3-Chloro-phenyl)-5-{1-[5-(4-methoxy-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,3,4]oxadiazole,

4-(5-{1-[5-(5-Chloro-2-fluoro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4-

methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

5-(5-Bromo-2-fluoro-phenyl)-3-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

2-(3-Chloro-phenyl)-5-[5-(4-methoxy-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,3,4]oxadiazole,

4-{5-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-cyclopropyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-cyclopropyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-(5-{1-[5-(2-Fluoro-5-methyl-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(4-Ethyl-5-{1-[5-(2-fluoro-5-methyl-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(4-Cyclopropyl-5-{1-[5-(2-fluoro-5-methyl-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(4-Cyclopropylmethyl-5-{1-[5-(2-fluoro-5-methyl-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4H-[1,2,4]triazol-3-yl)-pyridine,

2-(2-Fluoro-5-methyl-phenyl)-5-{1-[4-methyl-5-(2-methyl-thiazol-4-yl)-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,3,4]oxadiazole,

4-(5-{1-[5-(5-Chloro-2-fluoro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[5-(5-Chloro-2-fluoro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

2-(5-Chloro-2-fluoro-phenyl)-5-[1-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,3,4]oxadiazole,

2-(5-Chloro-2-fluoro-phenyl)-5-{1-[4-methyl-5-(2-methyl-thiazol-4-yl)-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,3,4]oxadiazole,

4-(4-Cyclopropylmethyl-5-{1-[5-(2-fluoro-5-methyl-phenyl)-isoxazol-3-yl]-ethylsulfanyl}-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[5-(3-Fluoro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(4-Cyclopropyl-5-{1-[5-(3-fluoro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[5-(4-Methoxy-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,3,4]oxadiazol-2-yl)-2-methyl-pyridine,

4-(5-{1-[4-Ethyl-5-(4-methoxy-phenyl)-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,3,4]oxadiazol-2-yl)-2-methyl-pyridine,

4-{5-[1-(4-Ethyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,3,4]oxadiazol-2-yl}-2-methyl-pyridine,

4-{5-[1-(4-Cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,3,4]oxadiazol-2-yl}-2-methyl-pyridine,

4-{5-[1-(5-Furan-2-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,3,4]oxadiazol-2-yl}-2-methyl-pyridine,

2-(3-Chloro-phenyl)-5-{1-[4-methyl-5-(2-methyl-thiazol-4-yl)-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,3,4]oxadiazole,

3-(5-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-2-methyl-pyridine,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

5-(3-Chloro-phenyl)-3-{1-[5-(4-methoxy-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,2,4]oxadiazole,

4-(5-{1-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

5-(5-Chloro-2-fluoro-phenyl)-3-{1-[5-(4-methoxy-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,2,4]oxadiazole,

4-[5-(4-Ethyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-2-methyl-pyridine,

4-[5-(4-Cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-2-methyl-pyridine,

4-{5-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-

cyclopropyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-[5-(5-Furan-2-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-2-methyl-pyridine,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4-cyclopropylmethyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[5-(4-Fluoro-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,3,4]oxadiazol-2-yl)-2-methyl-pyridine,

4-(5-{1-[5-(3-Fluoro-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,3,4]oxadiazol-2-yl)-2-methyl-pyridine,

3-[3-(4-Cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-4-fluoro-benzonitrile,

4-Chloro-2-[3-(4-cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-phenol,

4-{4-Cyclopropyl-5-[5-(3-methoxy-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{4-Cyclopropyl-5-[5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{4-Cyclopropyl-5-[5-(3-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

4-[4-Cyclopropyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine,

3-[3-(4-Cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzonitrile,

4-{4-Cyclopropyl-5-[5-(2,5-difluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

4-{4-Cyclopropyl-5-[1-(5-m-tolyl-[1,2,4]oxadiazol-3-yl)-ethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine,

4-(4-Cyclopropyl-5-{1-[5-(3-methoxy-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4H-[1,2,4]triazol-3-yl)-pyridine,

4-{5-[5-(2-Chloro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-cyclopropyl-4H-[1,2,4]triazol-3-yl}-pyridine,

2-[3-(4-Cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-4-methyl-phenol,

4-(5-{1-[5-(2-Chloro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

{3-[3-(4-Methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-phenyl}-methanol,

3-[5-(4-Methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-3-yl]-phenol,

5-(3-Chloro-phenyl)-3-[4-(tetrahydro-furan-2-ylmethyl)-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

(2-Chloro-phenyl)-{5-[5-(3-chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-isobutyl-4H-[1,2,4]triazol-3-yl}-methanol,

5-(2-Fluoro-5-methyl-phenyl)-3-[5-thiophen-2-yl-4-(2,2,2-trifluoro-ethyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

3-(2,5-Difluoro-phenyl)-5-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-Furan-3-yl-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-(3-Chloro-phenyl)-5-(5-furan-2-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-(3-Chloro-phenyl)-5-(5-furan-3-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(5-furan-2-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(5-furan-3-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyrimidine,

4-{5-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyrimidine,

3-(5-Chloro-2-fluoro-phenyl)-5-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-

ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-(5-Chloro-2-fluoro-phenyl)-5-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(5-Chloro-thiophen-2-yl)-3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(5-Chloro-thiophen-2-yl)-3-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(5-Chloro-thiophen-3-yl)-3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-ylmethoxy}-phenol,

4-{5-[5-(5-Chloro-2-fluoro-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-ylmethoxy}-phenol,

3-(2,5-Difluoro-phenyl)-5-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-(2,5-Difluoro-phenyl)-5-(5-furan-2-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

4-(5-{1-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-{5-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-cyclopropyl-4H-[1,2,4]triazol-3-yl}-pyrimidine,

2-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-5-methoxy-pyrimidine,

2-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyrimidine,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-2-methoxy-pyridine,

5-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-2-methoxy-pyridine,

2-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-5-methoxy-pyridine,

3-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-6-methoxy-pyridazine,

3-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-{5-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

5-(3-Chloro-phenyl)-3-(5-furan-2-yl-4-isobutyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-(3-methylsulfanyl-propyl)-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(4-hexyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(4-cyclopropylmethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-(3-fluoro-benzyl)-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-(3-methyl-benzyl)-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-(2-methyl-butyl)-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-(3-methyl-butyl)-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-[4-(2-fluoro-benzyl)-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-yloxymethyl)-[1,2,4]oxadiazole,

4-{5-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethoxy]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethoxy}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[3-(3-Chloro-phenyl)-isoxazol-5-yl]-ethoxy}-4-methyl-4H-[1,2,4]triazol-

3-yl)-pyridine,

5-(2-Methoxy-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-Furan-2-yl-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-[3-(4-Methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzoic acid methyl ester,

5-(2-Fluoro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(2,5-Difluoro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-(4-Methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-vinyl-phenyl)-[1,2,4]oxadiazole,

5-(3-Difluoromethoxy-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(4-Methoxy-thiophen-3-yl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(2-Chloro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(4-Fluoro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-(3-Chloro-phenyl)-5-[1-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,2,4]oxadiazole,

-(5-{1-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

3-(3-Chloro-phenyl)-5-[2-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-yl)-ethyl]-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(5-furan-2-yl-4-methyl-4H-[1,2,4]triazol-3-ylmethyl)-[1,2,4]oxadiazole,

2-(3-Chloro-phenyl)-5-[2-(5-furan-2-yl-4-methyl-4H-[1,2,4]triazol-3-yl)-ethyl]-[1,3,4]oxadiazole,

2-(3-Chloro-phenyl)-5-[2-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-yl)-ethyl]-[1,3,4]oxadiazole,

2-(3-Chloro-phenyl)-5-[2-(4-cyclopropyl-5-furan-2-yl-4H-[1,2,4]triazol-3-yl)-ethyl]-[1,3,4]oxadiazole,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-ethyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-ethyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-ethyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-2-methyl-propyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{2-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-propyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

8-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethyl]-3-pyridin-4-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridine,

8-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethyl]-3-thiophen-2-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridine,

8-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethyl]-3-pyridin-4-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridine,

5-(5-Bromo-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-(3-chloro-phenyl)-[1,2,4]oxadiazole,

3-[3-(4-Methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-phenylamine,

5-(3-Chloro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazole-3-sulfonylmethyl)-[1,2,4]oxadiazole,

5-(3-Chloro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazole-3-sulfinylmethyl)-[1,2,4]oxadiazole,

2-Methyl-6-[3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-

[1,2,4]oxadiazol-5-yl]-pyridine,

4-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyridin-2-ol,

4-(5-{2-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-propyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethyl]-methyl-(4-methyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-yl)-amine,

8-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethyl]-3-pyridin-4-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrimidine,

8-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethyl]-3-pyridin-4-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrimidine,

8-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-ylmethyl]-3-pyridin-4-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrimidine,

8-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethyl}-3-pyridin-4-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrimidine,

8-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethyl]-3-furan-2-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrimidine,

8-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethyl}-3-pyridin-4-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrimidine,

3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(1H-pyrrol-3-yl)-[1,2,4]oxadiazole,

4-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine 1-oxide,

5-(3-Chloro-phenyl)-3-(2-furan-2-yl-3-methyl-3H-imidazol-4-ylsulfanylmethyl)-[1,2,4]oxadiazole,

5-(5-Chloro-2-fluoro-phenyl)-3-[4-(2-fluoro-ethyl)-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole,

5-(5-Chloro-thiophen-3-yl)-3-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole,

3-[3-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-4-hydroxy-benzonitrile,

3-(3-Chloro-phenyl)-5-[2-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-yl)-ethyl]-[1,2,4]oxadiazole,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propyl}-[1,3,4]oxadiazol-2-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-1-methyl-ethyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-cyclopropyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine, or

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-1,1-dimethyl-ethyl}-[1,3,4]oxadiazol-2-yl)-pyridine,

3-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethoxy}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[5-(2-Chloro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[5-(2,5-Difluoro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{1-[5-(2-Fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(4-Cyclopropyl-5-{1-[5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4H-[1,2,4]triazol-3-yl)-pyridine,

3-{3-[1-(4-Methyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,2,4]oxadiazol-5-yl}-benzonitrile,

3-{3-[1-(4-Cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,2,4]oxadiazol-5-yl}-benzonitrile,

3-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-5-pyridin-4-yl-[1,2,4]triazol-4-ylamine,

3-(3-Chloro-phenyl)-5-[2-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-yl)-ethyl]-[1,2,4]oxadiazole,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-1-methyl-ethyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

cis-4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-cyclopropyl}-4-

cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-1,1-dimethyl-ethyl}-[1,3,4]oxadiazol-2-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-2-methyl-propyl}-[1,3,4]oxadiazol-2-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-1-methyl-ethyl}-[1,3,4]oxadiazol-2-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-cyclopropyl}-[1,3,4]oxadiazol-2-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-cyclopropyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{2-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-propyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propyl}-[1,3,4]oxadiazol-2-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

(S)-[1-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-2-(4-cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-yl)-ethyl]-carbamic acid tert-butyl ester,

(S)-1-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-2-(4-cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-yl)-ethylamine,

(S)-[1-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-2-(4-cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-yl)-ethyl]-dimethyl-amine,

and salts thereof.

[0166] Additional specific embodiments of the invention include:

4-(5-{2-[5-(3-chlorophenyl)-1,2,4-oxadiazol-3-yl]propyl}-4-cyclopropyl-4*H*-1,2,4-triazol-3-yl)pyridine,

4-[5-(chloromethyl)-4-methyl-4H-1,2,4-triazol-3-yl]pyridine,

4-(5-{2-[5-(3-chlorophenyl)-1,2,4-oxadiazol-3-yl]propyl}-4-cyclopropyl-4*H*-

1,2,4-triazol-3-yl)pyridine,

4-(5-{2-[5-(3-chlorophenyl)-1,2,4-oxadiazol-3-yl]ethyl}-4-cyclopropyl-4*H*-1,2,4-triazol-3-yl)pyridine,

4-(5-{2-[5-(3-chlorophenyl)-1,2,4-oxadiazol-3-yl]-1-methylethyl}-4-cyclopropyl-4H-1,2,4-triazol-3-yl)pyridine,

4-(5-{2-[5-(5-chloro-2-fluorophenyl)-1,2,4-oxadiazol-3-yl]propyl}-4-methyl-4H-1,2,4-triazol-3-yl)pyridine,

4-(5-{2-[5-(5-chloro-2-fluorophenyl)-1,2,4-oxadiazol-3-yl]propyl}-4-cyclopropyl-4H-1,2,4-triazol-3-yl)pyridine,

4-(4-methyl-5-{2-[5-(3-methylphenyl)-1,2,4-oxadiazol-3-yl]ethyl}-4H-1,2,4-triazol-3-yl)pyridine,

4-(4-cyclopropyl-5-{1-methyl-2-[5-(3-methylphenyl)-1,2,4-oxadiazol-3-yl]ethyl}-4H-1,2,4-triazol-3-yl)pyridine,

3-(3-Chloro-phenyl)-5-{2-[3-cyclopropyl-2-(4-methoxy-phenyl)-3H-imidazol-4-yl]-ethyl}-[1,2,4]oxadiazole,

3-(3-Chloro-phenyl)-5-{2-[3-cyclopropyl-2-(4-methoxy-phenyl)-3H-imidazol-4-yl]-1-methyl-ethyl}-[1,2,4]oxadiazole,

4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propyl}-1-cyclopropyl-1H-imidazol-2-yl)-pyridine,

3-(3-Chloro-phenyl)-5-{2-[2-(4-methoxy-phenyl)-3-methyl-3H-imidazol-4-yl]-1-methyl-ethyl}-[1,2,4]oxadiazole,

(S)-4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{(2S)-2-[5-(3-chlorophenyl)-1,3,4-oxadiazol-2-yl]propyl}-4-cyclopropyl-4H-1,2,4-triazol-3-yl)pyridine,

4-(5-{(2R)-2-[5-(3-chlorophenyl)-1,3,4-oxadiazol-2-yl]propyl}-4-cyclopropyl-4H-1,2,4-triazol-3-yl)pyridine,

4-(5-{1-[5-(3-chlorophenyl)-1,2,4-oxadiazol-3-yl]ethoxy}-4-methyl-4H-1,2,4-triazol-3-yl)pyridine,

5-(3-chlorophenyl)-3-((1R)-1-{[4-methyl-5-(trifluoromethyl)-4H-1,2,4-triazol-3-yl]oxy}ethyl)-1,2,4-oxadiazole,

3-(5-{1-[5-(3-chlorophenyl)-1,2,4-oxadiazol-3-yl]ethoxy}-4-cyclopropyl-4H-1,2,4-triazol-3-yl)pyridine,

3-(5-{(1*R*)-1-[5-(3-chlorophenyl)-1,2,4-oxadiazol-3-yl]ethoxy}-4-methyl-4*H*-1,2,4-triazol-3-yl)pyridine,

5-(3-chlorophenyl)-3-((1R)-1-{[5-(4-fluorophenyl)-4-methyl-4H-1,2,4-triazol-3-yl]oxy}ethyl)-1,2,4-oxadiazole,

5-(3-chlorophenyl)-3-((1*R*)-1-{[5-(3,5-difluorophenyl)-4-methyl-4*H*-1,2,4-triazol-3-yl]oxy}ethyl)-1,2,4-oxadiazole,

(+)-4-(5-{1-[5-(3-chlorophenyl)-1,2,4-oxadiazol-3-yl]propoxy}-4-methyl-4*H*-1,2,4-triazol-3-yl)pyridine,

(-)-4-(5-{(1R)-1-[5-(3-chlorophenyl)-1,2,4-oxadiazol-3-yl]ethoxy}-4-methyl-4H-1,2,4-triazol-3-yl)pyridine,

(+)-4-(5-{(1S)-1-[5-(3-chlorophenyl)-1,2,4-oxadiazol-3-yl]ethoxy}-4-methyl-4H-1,2,4-triazol-3-yl)pyridine,

(-)-4-(5-{1-[3-(3-chlorophenyl)-1,2,4-oxadiazol-5-yl]ethoxy}-4-methyl-4H-1,2,4-triazol-3-yl)pyridine,

(+)-4-(5-{1-[3-(3-chlorophenyl)-1,2,4-oxadiazol-5-yl]ethoxy}-4-methyl-4H-1,2,4-triazol-3-yl)pyridine,

4-(5-{1-[5-(3-Chloro-phenyl)-isoxazol-3-yl]-ethoxy}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

N-{1-[5-(3-chlorophenyl)-1,2,4-oxadiazol-3-yl]ethyl}-*N*,4-dimethyl-5-pyridin-3-yl-4*H*-1,2,4-triazol-3-amine,

3-Pyridin-4-yl-8-[1-(5-m-tolyl-[1,2,4]oxadiazol-3-yl)-ethyl]-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrimidine,

N,4-dimethyl-*N*-{[5-(3-methylphenyl)-1,2,4-oxadiazol-3-yl]methyl}-5-pyridin-4-yl-4*H*-1,2,4-triazol-3-amine,

N-{[5-(5-chloro-2-fluorophenyl)-1,2,4-oxadiazol-3-yl]methyl}-*N*,4-dimethyl-5-pyridin-4-yl-4*H*-1,2,4-triazol-3-amine,

N-{[5-(4-chlorophenyl)-1,2,4-oxadiazol-3-yl]methyl}-*N*-cyclopropyl-4-methyl-5-pyridin-4-yl-4*H*-1,2,4-triazol-3-amine,

(+)-*N*-{1-[5-(3-chlorophenyl)-1,2,4-oxadiazol-3-yl]ethyl}-5-(3,5-difluorophenyl)-

N,4-dimethyl-4*H*-1,2,4-triazol-3-amine,

(-)-*N*-{1-[5-(3-chlorophenyl)-1,2,4-oxadiazol-3-yl]ethyl}-5-(3,5-difluorophenyl)-*N*,4-dimethyl-4*H*-1,2,4-triazol-3-amine,

(+)-8-{(1S)-1-[5-(3-chlorophenyl)-1,2,4-oxadiazol-3-yl]ethyl}-3-pyridin-4-yl-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyrimidine,

(-)-8-{(1R)-1-[5-(3-chlorophenyl)-1,2,4-oxadiazol-3-yl]ethyl}-3-pyridin-4-yl-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyrimidine,

(-)-N-{1-[3-(3-chlorophenyl)-1,2,4-oxadiazol-5-yl]ethyl}-N,4-dimethyl-5-pyridin-4-yl-4H-1,2,4-triazol-3-amine,

(+)-N-{1-[3-(3-chlorophenyl)-1,2,4-oxadiazol-5-yl]ethyl}-N,4-dimethyl-5-pyridin-4-yl-4H-1,2,4-triazol-3-amine,

(-)-N-{(1S)-1-[5-(3-chlorophenyl)-1,2,4-oxadiazol-3-yl]ethyl}-N,4-dimethyl-5-pyridin-4-yl-4H-1,2,4-triazol-3-amine,

(+)-N-{(1R)-1-[5-(3-chlorophenyl)-1,2,4-oxadiazol-3-yl]ethyl}-N,4-dimethyl-5-pyridin-4-yl-4H-1,2,4-triazol-3-amine,

3-[5-(3-Pyridin-4-yl-6,7-dihydro-5*H*-[1,2,4]triazolo[4,3-*a*]pyrimidin-8-ylmethyl)[1,3,4]oxadiazol-2-yl]benzonitrile,

3-{5-[3-(2-Methoxypyridin-4-yl)-6,7-dihydro-5*H*-[1,2,4]triazolo[4,3-*a*]pyrimidin-8-ylmethyl][1,3,4]oxadiazol-2-yl}benzonitrile,

3-(5-{[Methyl-(4-methyl-5-pyridin-4-yl-4*H*-[1,2,4]triazol-3-yl)-amino]-methyl}[1,3,4]oxadiazol-2-yl)benzonitrile,

3-{5-[3-(2-Methoxy-pyridin-4-yl)-6,7-dihydro-5H-[1,2,4]triazolo[4,3-a]pyrimidin-8-ylmethyl]-[1,2,4]oxadiazol-3-yl}-benzonitrile,

3-{3-[(3-pyridin-4-yl-6,7-dihydro[1,2,4]triazolo[4,3-*a*]pyrimidin-8(5*H*)-yl)methyl]-1,2,4-oxadiazol-5-yl}benzonitrile,

3-(3-{[[5-(2-methoxypyridin-4-yl)-4-methyl-4*H*-1,2,4-triazol-3-yl](methyl)amino]methyl}-1,2,4-oxadiazol-5-yl)benzonitrile,

3-(3-{[methyl(4-methyl-5-pyridin-4-yl-4*H*-1,2,4-triazol-3-yl)amino]methyl}-1,2,4-oxadiazol-5-yl)benzonitrile,

3-(3-{[3-(2-methoxypyridin-4-yl)-6,7-dihydro[1,2,4]triazolo[4,3-*a*]pyrimidin-8(5*H*)-yl]methyl}-1,2,4-oxadiazol-5-yl)benzonitrile,

N-{1-[5-(3-chlorophenyl)-1,2,4-oxadiazol-3-yl]ethyl}-N,4-dimethyl-5-pyridin-4-yl-4H-1,2,4-triazol-3-amine,

3-{5-[(3-pyridin-4-yl-6,7-dihydro[1,2,4]triazolo[4,3-a]pyrimidin-8(5H)-yl)methyl]-1,2,4-oxadiazol-3yl}benzonitrile,

3-{5-[3-(2-Hydroxy-pyridin-4-yl)-6,7-dihydro-5H-[1,2,4]triazolo[4,3-a]pyrimidin-8-ylmethyl]-[1,2,4]oxadiazol-3-yl}-benzonitrile,

N-{[3-(3-chlorophenyl)-1,2,4-oxadiazol-5-yl]methyl}-N,4-dimethyl-5-pyridin-4-yl-4H-1,2,4-triazol-3-amine,

N-{[3-(3-Chlorophenyl)-1,2,4-oxadiazol-5-yl]methyl}-4-cyclopropyl-N-methyl-5-pyridin-4-yl-4H-1,2,4-triazol-3-amine,

[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-ylmethyl]-ethyl-(4-methyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-yl)-amine,

[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-ylmethyl]-ethyl-(4-methyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-yl)-amine,

N-{[3-(3-Chlorophenyl)-1,2,4-oxadiazol-5-yl]methyl}-N-isopropyl-4-methyl-5-pyridin-4-yl-4H-1,2,4-triazol-3-amine,

N-{1-[3-(3-Chlorophenyl)-1,2,4-oxadiazol-5-yl]ethyl}-N-cyclopropyl-4-methyl-5-pyridin-4-yl-4H-1,2,4-triazol-3-amine,

{1-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-ethyl}-methyl-(4-methyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-yl)-amine,

[5-(3-Chloro-phenyl)-isoxazol-3-ylmethyl]-methyl-(4-methyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-yl)-amine,

N-{[5-(3-chlorophenyl)-1,2,4-oxadiazol-3-yl]methyl}-4-cyclopropyl-*N*-methyl-5-pyridin-4-yl-4*H*-1,2,4-triazol-3-amine,

N-{1-[5-(3-chlorophenyl)-1,2,4-oxadiazol-3-yl]-1-methylethyl}-N,4-dimethyl-5-pyridin-4-yl-4H-1,2,4-triazol-3-amine,

4-(5-{1-[5-(3-chlorophenyl)-1,2,4-oxadiazol-3-yl]-1-methylethoxy}-4-methyl-4H-1,2,4-triazol-3-yl)pyridine,

N-{(1S)-1-[5-(3-chlorophenyl)-1,2,4-oxadiazol-3-yl]ethyl}-4-methyl-5-pyridin-4-yl-4H-1,2,4-triazol-3-amine,

5-(3-chlorophenyl)-N-methyl-N-[(4-methyl-5-pyridin-4-yl-4H-1,2,4-triazol-3-

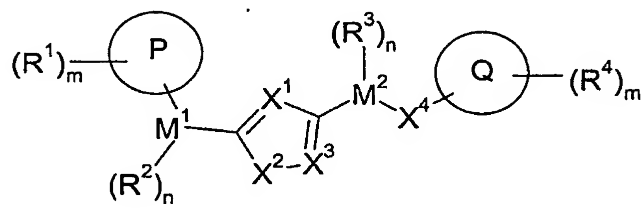
yl)methyl]-1,2,4-oxadiazol-3-amine,

5-(3-chlorophenyl)-N-ethyl-N-[(4-methyl-5-pyridin-4-yl-4H-1,2,4-triazol-3-yl)methyl]-1,2,4-oxadiazol-3-amine,

[0167] Ethyl 8-{1-[5-(3-chlorophenyl)-1,2,4-oxadiazol-3-yl]ethyl}-3-pyridin-4-yl-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridine-8-carboxylate,

and salts thereof.

[0168] Further feasible examples of compounds of formula I are provided by compounds of formula Ia



(Ia)

wherein:

[0169] P is selected from the group consisting of hydrogen, C_{3-7}alkyl and a 3- to 8-membered ring containing one or more atoms independently selected from the group consisting of C, N, O and S, which ring may optionally be fused with a 5- or 6-membered ring containing one or more atoms independently selected from the group consisting of C, N, O and S;

[0170] R^1 is selected from the group consisting of hydrogen, hydroxy, halo, nitro, C_{1-6}alkylhalo, OC_{1-6}alkylhalo, C_{1-6}alkyl, OC_{1-6}alkyl, C_{2-6}alkenyl, OC_{2-6}alkenyl, C_{2-6}alkynyl, OC_{2-6}alkynyl, C_{0-6}alkylC_{3-6}cycloalkyl, OC_{0-6}alkylC_{3-6}cycloalkyl, C_{0-6}alkylaryl, OC_{0-6}alkylaryl, CHO, $(CO)R^5$, $O(CO)R^5$, $O(CO)OR^5$, $O(CN)OR^5$, C_{1-6}alkylOR^5, OC_{2-6}alkylOR^5, C_{1-6}alkyl$(CO)R^5$, OC_{1-6}alkyl$(CO)R^5$, C_{0-6}alkylCO_2R^5, OC_{1-6}alkylCO_2R^5, C_{0-6}alkylcyano, OC_{2-6}alkylcyano, C_{0-6}alkylNR^5R^6, OC_{2-6}alkylNR^5R^6, C_{1-6}alkyl$(CO)NR^5R^6$, OC_{1-6}alkyl$(CO)NR^5R^6$, C_{0-6}alkyl$NR^5(CO)R^6$, OC_{2-6}alkyl$NR^5(CO)R^6$, C_{0-6}alkyl$NR^5(CO)NR^5R^6$, C_{0-6}alkylSR^5, OC_{2-6}alkylSR^5, C_{0-6}alkyl$(SO)R^5$, OC_{2-6}alkyl$(SO)R^5$, C_{0-6}alkylSO_2R^5, OC_{2-6}alkylSO_2R^5, C_{0-6}alkyl$(SO_2)NR^5R^6$, OC_{2-6}alkyl$(SO_2)NR^5R^6$,C_{0-6}alkyl$NR^5(SO_2)R^6$, OC_{2-6}alkyl$NR^5(SO_2)R^6$, C_{0-6}alkyl$NR^5(SO_2)NR^5R^6$, OC_{2-6}alkyl$NR^5(SO_2)NR^5R^6$, $(CO)NR^5R^6$, $O(CO)NR^5R^6$, NR^5OR^6, C_{0-6}alkyl$NR^5(CO)OR^6$, OC_{2-}

$_6$alkylNR^5(CO)OR^6, SO$_3$R^5 and a 5- or 6-membered ring containing one or more atoms independently selected from the group consisting of C, N, O and S, wherein said ring may be substituted by one or more A;

[0171] M^1 is selected from the group consisting of a bond, C$_{1-3}$alkyl, C$_{2-3}$alkenyl, C$_{2-3}$alkynyl, C$_{0-4}$alkyl(CO)C$_{0-4}$alkyl, C$_{0-3}$alkylOC$_{0-3}$alkyl, C$_{0-3}$alkyl(CO)NR^5, C$_{0-3}$alkyl(CO)NR^{5}C$_{0-3}$alkyl, C$_{0-4}$alkylNR^5, C$_{0-3}$alkylSC$_{0-3}$alkyl, C$_{0-3}$alkyl(SO)C$_{0-3}$alkyl and C$_{0-3}$alkyl(SO$_2$)C$_{0-3}$alkyl;

[0172] R^2 is selected from the group consisting of hydrogen, hydroxy, C$_{0-6}$alkylcyano, oxo, =NR^5, =NOR^5, C$_{1-4}$alkylhalo, halo, C$_{1-4}$alkyl, O(CO)C$_{1-4}$alkyl, C$_{1-4}$alkyl(SO)C$_{0-4}$alkyl, C$_{1-4}$alkyl(SO$_2$)C$_{0-4}$alkyl, (SO)C$_{0-4}$alkyl, (SO$_2$)C$_{0-4}$alkyl, OC$_{1-4}$alkyl, , C$_{1-4}$alkylOR^5 and C$_{0-4}$alkylNR^{5}R^6;

[0173] X^1, X^2 and X^3 are independently selected from the group consisting of CR, CO, N, NR, O and S;

[0174] R is selected from the group consisting of hydrogen, C$_{0-3}$alkyl, halo, C$_{0-3}$alkylOR^5, C$_{0-3}$alkylNR^{5}R^6, C$_{0-3}$alkyl(CO)OR^5, C$_{0-3}$alkylNR^{5}R^6 and C$_{0-3}$alkylaryl;

[0175] M^2 is selected from the group consisting of a bond, C$_{1-3}$alkyl, C$_{3-7}$cycloalkyl, C$_{2-3}$alkenyl, C$_{2-3}$alkynyl, C$_{0-4}$alkyl(CO)C$_{0-4}$alkyl, C$_{0-3}$alkylOC$_{0-3}$alkyl, C$_{0-3}$alkylNR^{5}C$_{1-3}$alkyl, C$_{0-3}$alkyl(CO)NR^5, C$_{0-4}$alkylNR^5, C$_{0-3}$alkylSC$_{0-3}$alkyl, C$_{0-3}$alkyl(SO)C$_{0-3}$alkyl and C$_{0-3}$alkyl(SO$_2$)C$_{0-3}$alkyl;

[0176] R^3 is selected from the group consisting of hydrogen, hydroxy, C$_{0-6}$alkylcyano, oxo, =NR^5, =NOR^5, C$_{1-4}$alkylhalo, halo, C$_{1-4}$alkyl, O(CO)C$_{1-4}$alkyl, C$_{1-4}$alkyl(SO)C$_{0-4}$alkyl, C$_{1-4}$alkyl(SO$_2$)C$_{0-4}$alkyl, (SO)C$_{0-4}$alkyl, (SO$_2$)C$_{0-4}$alkyl, OC$_{1-4}$alkyl, C$_{1-4}$alkylOR^5 and C$_{0-4}$alkylNR^{5}R^6;

[0177] X^4 is selected from the group consisting of C$_{0-4}$alkylR^5, C$_{0-4}$alkyl(NR^{5}R^6), C$_{0-4}$alkyl(NR^{5}R^6)=N, NR^{5}C$_{0-4}$alkyl(NR^{5}R^6)=N, NOC$_{0-4}$alkyl, C$_{1-4}$alkylhalo, C, O, SO, SO$_2$ and S;

[0178] Q is a 5- or 6-membered ring containing one or more atoms independently selected from C, N, O and S, which group may optionally be fused with a 5- or 6-membered ring containing one or more atoms independently selected from C, N, O and S and which fused ring may be substituted by one or more A;

[0179] R^4 is selected from the group consisting of hydrogen, hydroxy, C$_{0-}$

$_{6}$alkylcyano, oxo, =NR^5, =NOR^5, C_{1-4}alkylhalo, halo, C_{1-4}alkyl, OC_{1-4}alkyl, OC_{0-6}alkylaryl, O(CO)C_{1-4}alkyl, C_{0-4}alkyl(S)C_{0-4}alkyl, C_{1-4}alkyl(SO)C_{0-4}alkyl, C_{1-4}alkyl(SO_2)C_{0-4}alkyl, (SO)C_{0-4}alkyl, (SO_2)C_{0-4}alkyl, C_{1-4}alkylOR^5, C_{0-4}alkylNR^{5}R^6 and a 5- or 6-membered ring containing one or more atoms independently selected from C, N, O and S, wherein said ring may be substituted by one or more A;

[0180] R^5 and R^6 are independently selected from the group consisting of hydrogen, hydroxy, C_{1-6}alkyl, C_{0-6}alkylC_{3-6}cycloalkyl, C_{0-6}alkylaryl, C_{0-6}alkylheteroaryl and a 5- or 6-membered ring containing one or more atoms independently selected from C, N, O and S, and wherein R^5 and R^6 may together form a 5- or 6-membered ring containing one or more atoms independently selected from C, N, O and S;

[0181] wherein any C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{0-6}alkylC_{3-6}cycloalkyl, C_{0-6}alkylaryl and C_{0-6}alkylheteroaryl defined under R^1, R^2, R^3, R^4, R^5 and R^6 may be substituted by one or more A; and

[0182] A is selected from the group consisting of hydrogen, hydroxy, oxo, halo, nitro, C_{0-6}alkylcyano, C_{1-4}alkyl, C_{0-4}alkylC_{3-6}cycloalkyl, C_{1-6}alkylhalo, OC_{1-6}alkylhalo, C_{2-6}alkenyl, OC_{1-6}alkyl, C_{0-3}alkylaryl, C_{0-6}alkylOR^5, OC_{2-6}alkylOR^5, C_{1-6}alkylSR^5, OC_{2-6}alkylSR^5, (CO)R^5, O(CO)R^5, OC_{2-6}alkylcyano, C_{0-6}alkylCO_2R^5, OC_{1-6}alkylCO_2R^5, O(CO)OR^5, OC_{1-6}alkyl(CO)R^5, C_{1-6}alkyl(CO)R^5, NR^{5}OR^6, C_{0-6}alkylNR^{5}R^6, OC_{2-6}alkylNR^{5}R^6, C_{0-6}alkyl(CO)NR^{5}R^6, OC_{1-6}alkyl(CO)NR^{5}R^6, OC_{2-6}alkylNR^5(CO)R^6, C_{0-6}alkylNR^5(CO)R^6, C_{0-6}alkylNR^5(CO)NR^{5}R^6, O(CO)NR^{5}R^6, NR^5(CO)OR^6, C_{0-6}alkyl(SO_2)NR^{5}R^6, OC_{2-6}alkyl(SO_2)NR^{5}R^6, C_{0-6}alkylNR^5(SO_2)R^6, OC_{2-6}alkylNR^5(SO_2)R^6, SO_3R^5, C_{1-6}alkylNR^5(SO_2)NR^{5}R^6, OC_{2-6}alkyl(SO_2)R^5, C_{0-6}alkyl(SO_2)R^5, C_{0-6}alkyl(SO)R^5, OC_{2-6}alkyl(SO)R^5 and a 5- or 6-membered ring containing one or more atoms independently selected from C, N, O and S;

[0183] m is selected from 0, 1, 2, 3 and 4; and

[0184] n is selected from 0, 1, 2 and 3,

[0185] or salt thereof.

[0186] The present invention relates to the use of compounds of formula I and IA as hereinbefore defined as well as to the salts thereof. Salts for use in pharmaceutical formulations will be pharmaceutically acceptable salts, but other salts may be useful in the production of the compounds of formula I and Ia.

[0187] Examples of pharmaceutically acceptable salts may be, but are not limited to hydrochloride, 4-aminobenzoate, anthranilate, 4-aminosalicylate, 4-hydroxybenzoate, 3,4-dihydroxybenzoate, 3-hydroxy-2-naphthoate, nitrate and trifluoroacetate. Other pharmaceutically acceptable salts and methods of preparing these salts may be found in, for example, Remington's Pharmaceutical Sciences (18^{th} Edition, Mack Publishing Co.).

[0188] Some compounds of formula I may have chiral centres and/or geometric isomeric centres (E- and Z- isomers), and it is to be understood that the invention encompasses all such optical, diastereoisomers and geometric isomers.

[0189] The invention relates to any and all tautomeric forms of the compounds of formula I.

[0190] The invention relates to the following compounds, which may be used as intermediates in the preparation of a compound of formula I;

6-Methylpyridine-4-carboxylic acid,
1-Cyano-3-ethylbenzene,
3-Ethylbenzoic acid,
3-Fluoro-5-methyl-benzoic acid,
3-Methoxymethyl-benzoic acid,
N-Hydroxy-3-methoxy-benzamidine,
N-Hydroxy-benzamidine,
N-Hydroxy-3-methyl-benzamidine,
5-Chloromethyl-3-(3-methoxy-phenyl)-[1,2,4]oxadiazole,
5-Chloromethyl-3-phenyl-[1,2,4]oxadiazole,
5-Chloromethyl-3-m-tolyl-[1,2,4]oxadiazole,
3-(3-Chloromethyl-[1,2,4]oxadiazol-5-yl)-benzonitrile,
3-(5-Chloromethyl-[1,2,4]oxadiazol-3-yl)-benzonitrile,
3-Chloromethyl-5-m-tolyl-[1,2,4]oxadiazole,
3-Chloromethyl-5-(3-fluoro-phenyl)-[1,2,4]oxadiazole,
3-Chloromethyl-5-thiophen-3-yl-[1,2,4]oxadiazole,
3-(3-Chloromethyl-[1,2,4]oxadiazol-5-yl)-5-methyl-pyridine,
3-Chloromethyl-5-(3-nitro-phenyl)-[1,2,4]oxadiazole,

4-(3-Chloromethyl-[1,2,4]oxadiazol-5-yl)-2-methyl-pyridine,

3-Chloromethyl-5-(3-ethyl-phenyl)-[1,2,4]oxadiazole,

3-(3-Chloromethyl-[1,2,4]oxadiazol-5-yl)-phenyl]-dimethyl-amine,

3-Chloromethyl-5-(3-chloro-phenyl)-[1,2,4]oxadiazole,

3-Chloromethyl-5-(3-trifluoromethoxy-phenyl)-[1,2,4]oxadiazole,

5-(3-Bromo-phenyl)-3-chloromethyl-[1,2,4]oxadiazole,

3-Chloromethyl-5-thiophen-2-yl-[1,2,4]oxadiazole,

3-Chloromethyl-5-(3-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazole,

3-Chloromethyl-5-thiazol-4-yl-[1,2,4]oxadiazole,

3-Chloromethyl-5-(3-iodo-phenyl)-[1,2,4]oxadiazole,

3-Chloromethyl-5-(3-methoxymethyl-phenyl)-[1,2,4]oxadiazole,

5-Furan-2-yl-4-methyl-4*H*-[1,2,4]triazole-3-thiol,

4-Methyl-5-phenyl-4*H*-[1,2,4]triazole-3-thiol,

4-Methyl-5-pyridin-2-yl-4H-[1,2,4]triazole-3-thiol,

5-(4-Benzyl-morpholin-2-yl)-4-methyl-4*H*-[1,2,4]triazole-3-thiol,

5-tert-Butyl-4-methyl-4*H*-[1,2,4]triazole-3-thiol,

4-Methyl-5-pyridin-3-yl-4*H*-[1,2,4]triazole-3-thiol,

4-Methyl-5-thiophene-3-yl-4*H*-[1,2,4]triazole-3-thiol,

4-Methyl-5-thiazol-4-yl-4*H*-[1,2,4]triazole-3-thiol,

5-Cyclohexyl-4-methyl-4*H*-[1,2,4]triazole-3-thiol,

5-Chloro-thiophene-3-carboxylic acid,

3-Methylsulfanyl-benzoic acid,

3-Cyclopropyl-benzoic acid,

3-tert-Butoxycarbonylamino-benzoic acid,

3-Acetyl-benzoic acid,

2-Methyl-isonicotinic acid hydrazide,

5-Chloro-2-fluoro-benzoic acid hydrazide.,

3-Cyano-benzoic acid hydrazide,

2-Chloro-isonicotinic acid hydrazide,

2-Fluoro-5-methyl-benzoic acid hydrazide ,

Pyrimidine-4-carboxylic acid hydrazide,

3-Fluoro-N-hydroxy-benzamidine,

N-Hydroxy-thiophene-3-carboxamidine,

2-Chloro-N-hydroxy-propionamidine ,

3,N-Dihydroxy-benzamidine,

N-Hydroxy-2-methyl-benzamidine,

N-Hydroxy-2-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-acetamidine,

3-Chloro-N-hydroxy-benzamidine ,

N-Hydroxy-2-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-acetamidine,

2,5-Difluoro-N-hydroxy-benzamidine,

4-Methyl-5-pyridin-3-yl-4H-[1,2,4]triazole-3-thiol,

4-Butyl-5-thiophen-2-yl-4H-[1,2,4]triazole-3-thiol,

4-(3-Methoxy-propyl)-5-thiophen-2-yl-4H-[1,2,4]triazole-3-thiol ,

4-Benzyl-5-thiophen-2-yl-4H-[1,2,4]triazole-3-thiol ,

4-Furan-2-ylmethyl-5-thiophen-2-yl-4H-[1,2,4]triazole-3-thiol ,

5-Thiophen-2-yl-4-thiophen-2-ylmethyl-4H-[1,2,4]triazole-3-thiol ,

4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazole-3-thiol ,

4-Furan-2-ylmethyl-5-pyridin-4-yl-4H-[1,2,4]triazole-3-thiol ,

4-Ethyl-5-pyridin-4-yl-4H-[1,2,4]triazole-3-thiol ,

4-Ethyl-5-pyridin-3-yl-4H-[1,2,4]triazole-3-thiol ,

4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazole-3-thiol ,

4-Furan-2-ylmethyl-5-pyridin-3-yl-4H-[1,2,4]triazole-3-thiol ,

4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazole-3-thiol ,

4-Ethyl-5-(3-fluoro-phenyl)-4H-[1,2,4]triazole-3-thiol ,

4-Ethyl-5-(4-fluoro-phenyl)-4H-[1,2,4]triazole-3-thiol ,

5-(2-Fluoro-5-methyl-phenyl)-4-furan-2-ylmethyl-4H-[1,2,4]triazole-3-thiol ,

4-Ethyl-5-(3-methyl-thiophen-2-yl)-4H-[1,2,4]triazole-3-thiol ,

4-Ethyl-5-(5-methyl-thiophen-2-yl)-4H-[1,2,4]triazole-3-thiol ,

5-(2-Chloro-6-methyl-pyridin-4-yl)-4-ethyl-4H-[1,2,4]triazole-3-thiol ,

5-(5-Bromo-furan-2-yl)-4-ethyl-4H-[1,2,4]triazole-3-thiol ,

4-Ethyl-5-(3-methoxy-thiophen-2-yl)-4H-[1,2,4]triazole-3-thiol ,
4-Ethyl-5-(tetrahydro-furan-2-yl)-2,4-dihydro-[1,2,4]triazole-3-thione,
4-Ethyl-5-thioxo-4,5-dihydro-1H-[1,2,4]triazole-3-carboxylic acid methyl ester,
5-(2-Chloro-pyridin-4-yl)-4-ethyl-4H-[1,2,4]triazole-3-thiol ,
5-(2-Chloro-6-methoxy-pyridin-4-yl)-4-ethyl-4H-[1,2,4]triazole-3-thiol ,
4-Ethyl-5-(3-methyl-3H-imidazol-4-yl)-4H-[1,2,4]triazole-3-thiol,
4-Propyl-5-pyridin-4-yl-4H-[1,2,4]triazole-3-thiol ,
4-Ethyl-5-(1-methyl-1H-imidazol-2-yl)-4H-[1,2,4]triazole-3-thiol ,
4-Ethyl-5-(1-methyl-1H-imidazol-4-yl)-4H-[1,2,4]triazole-3-thiol,
3-(5-Mercapto-4-methyl-4H-[1,2,4]triazol-3-yl)-benzonitrile,
5-(3-Chloro-phenyl)-4-methyl-4H-[1,2,4]triazole-3-thiol,
5-(4-Chloro-phenyl)-4-methyl-4H-[1,2,4]triazole-3-thiol,
5-(2-fluoro-phenyl)-4-methyl-4H-[1,2,4]triazole-3-thiol,
5-(3-fluoro-phenyl)-4-methyl-4H-[1,2,4]triazole-3-thiol,
5-(4-fluoro-phenyl)-4-methyl-4H-[1,2,4]triazole-3-thiol,
5-Benzo[b]thiophen-2-yl-4-methyl-4H-[1,2,4]triazole-3-thiol,
5-(3-methoxy-phenyl)-4-methyl-4H-[1,2,4]triazole-3-thiol,
5-(4-methoxy-phenyl)-4-methyl-4H-[1,2,4]triazole-3-thiol,
4-Ethyl-5-(4-methoxy-phenyl)-4H-[1,2,4]triazole-3-thiol ,
5-(3,5-Difluoro-phenyl)-4-ethyl-4H-[1,2,4]triazole-3-thiol ,
5-(2,6-Difluoro-phenyl)-4-ethyl-4H-[1,2,4]triazole-3-thiol,
5-(4-Butoxy-phenyl)-4-ethyl-4H-[1,2,4]triazole-3-thiol ,
5-Benzo[1,3]dioxol-5-yl-4-ethyl-4H-[1,2,4]triazole-3-thiol ,
4-Ethyl-5-pyrimidin-5-yl-2,4-dihydro-[1,2,4]triazole-3-thione,
4-Ethyl-5-furan-3-yl-2,4-dihydro-[1,2,4]triazole-3-thione,
4-(Tetrahydrofuran-2-ylmethyl)-5-thiophene-2-yl-2,4-dihydro-[1,2,4]triazole-3-thione,
5-Cyclopentyl-4-ethyl-2,4-dihydro-[1,2,4]triazole-3-thione,
4-Ethyl-5-[2-(4-methoxy-phenyl)-ethyl]-2,4-dihydro-[1,2,4]triazole-3-thione,
5-(3,5-Dichloro-phenyl)-4-ethyl-4H-[1,2,4]triazole-3-thiol,
5-(3-Methylphenyl)-4-ethyl-4H-[1,2,4]triazole-3-thiol,

5-(4-Methylphenyl)-4-ethyl-4H-[1,2,4]triazole-3-thiol,

4-Ethyl- 5-(3-nitrophenyl)-4H-[1,2,4]triazole-3-thiol,

5-(2,5-Difluorophenyl)-4-ethyl-4H-[1,2,4]triazole-3-thiol,

5-(3-Chlorophenyl)-4-ethyl-4H-[1,2,4]triazole-3-thiol,

5-(4-Chlorophenyl)-4-ethyl-4H-[1,2,4]triazole-3-thiol,

4-Ethyl-5-methoxymethyl-2,4-dihydro-[1,2,4]triazole-3-thione,

4-Methyl-5-pyridin-4-yl-2,4-dihydro-[1,2,4]triazole-3-thione,

4-Allyl-5-furan-2-yl-2,4-dihydro-[1,2,4]triazole-3-thione,

4-Ethyl-5-(4-methoxy-phenoxymethyl)-2,4-dihydro-[1,2,4]triazole-3-thione,

4-Ethyl-5-phenoxymethyl-2,4-dihydro-[1,2,4]triazole-3-thione,

4-Ethyl-5-hydroxymethyl-2,4-dihydro-[1,2,4]triazole-3-thione,

4-Ethyl-5-(2-methoxy-ethyl)-2,4-dihydro-[1,2,4]triazole-3-thione,

4-Ethyl-5-methylsulfanylmethyl-2,4-dihydro-[1,2,4]triazole-3-thione,

5-Ethoxymethyl-4-ethyl-2,4-dihydro-[1,2,4]triazole-3-thione,

5-Furan-3-yl-4-methyl-2,4-dihydro-[1,2,4]triazole-3-thione ,

4-Methyl-5-pyrimidin-4-yl-2,4-dihydro-[1,2,4]triazole-3-thione,

4-Ethyl-5-pyridazin-4-yl-2,4-dihydro-[1,2,4]triazole-3-thione,

4-Ethyl-5-pyridin-4-ylmethyl-2,4-dihydro-[1,2,4]triazole-3-thione,

4-Ethyl-5-(6-hydroxy-pyridin-3-yl)-2,4-dihydro-[1,2,4]triazole-3-thione,

4-Ethyl-5-(4-hydroxy-phenyl)-2,4-dihydro-[1,2,4]triazole-3-thione,

4-Ethyl-5-p-tolyloxymethyl-2,4-dihydro-[1,2,4]triazole-3-thione,

4-Ethyl-5-(6-methoxy-pyridin-3-yl)-2,4-dihydro-[1,2,4]triazole-3-thione,

4-Ethyl-5-(2-methoxy-pyridin-4-yl)-2,4-dihydro-[1,2,4]triazole-3-thione,

4-Ethyl-5-pyrimidin-2-yl-2,4-dihydro-[1,2,4]triazole-3-thione,

4-Ethyl-5-(5-methoxy-pyrimidin-2-yl)-2,4-dihydro-[1,2,4]triazole-3-thione,

4-Furan-2-ylmethyl-4H-[1,2,4]triazole-3-thiol,

4-Cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazole-3-thiol,

4-Cyclopropylmethyl-5-pyridin-4-yl-4H-[1,2,4]triazole-3-thiol,

4-Cyclopropyl-5-thiophen-2-yl-2,4-dihydro-[1,2,4]triazole-3-thione,

5-Furan-2-yl-4-(2-methoxy-ethyl)-2,4-dihydro-[1,2,4]triazole-3-thione,

4-Cyclopropyl-5-furan-2-yl-2,4-dihydro-[1,2,4]triazole-3-thione,

(3-Thiophen-2-yl-5-thioxo-1,5-dihydro-[1,2,4]triazol-4-yl)-acetic acid methyl ester,

4-Cyclopropylmethyl-5-thiophene-2-yl-2,4-dihydro-[1,2,4]triazole-3-thione,

4-(2-Methoxy-ethyl)-5-thiophen-2-yl-2,4-dihydro-[1,2,4]triazole-3-thione,

Thiophen-2-yl-4-(2,2,2-trifluoroethyl)-2,4-dihydro-[1,2,4]triazole-3-thione,

4-Cyclopropyl-5-pyrimidin-4-yl-2,4-dihydro-[1,2,4]triazole-3-thione,

4-Cyclopropyl-5-pyridin-3-yl-2,4-dihydro-[1,2,4]triazole-3-thione,

4-Ethyl-5-trifluoromethyl-4H-[1,2,4]triazole-3-thiol,

4-Ethyl-3-methanesulfonyl-5-thiophen-2-yl-4H-[1,2,4]triazole,

4-(5-Methanesulfonyl-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(2-Hydroxy-ethyl)-5-thiophen-2-yl-2,4-dihydro-[1,2,4]triazole-3-thione,

4-(4,5-Dimethyl-4H-[1,2,4]triazol-3-yl)-pyridine,

Methyl-(4-methyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-yl)-amine,

3-Pyridin-4-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrimidine,

3-Furan-2-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3- a]pyrimidine,

4-Ethyl-5-(6-methoxy-pyridazin-3-yl)-2,4-dihydro-[1,2,4]triazole-3-thione,

4-Ethyl-5-(5-methoxy-pyridin-2-yl)-2,4-dihydro-[1,2,4]triazole-3-thione,

5-Chloromethyl-3-phenyl-[1,2,4]oxadiazole,

5-Chloromethyl-3-(3-fluoro-phenyl)-[1,2,4]oxadiazole,

5-Chloromethyl-3-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazole ,

5-Chloromethyl-3-thiophen-2-yl-[1,2,4]oxadiazole,

5-Chloromethyl-3-thiophen-3-yl-[1,2,4]oxadiazole,

3-(5-Chloromethyl-[1,2,4]oxadiazol-3-yl)-phenol,

5-Chloromethyl-3-o-tolyl-[1,2,4]oxadiazole,

5-Chloromethyl-3-(3-chloro-phenyl)-[1,2,4]oxadiazole,

5-Chloromethyl-3-(2,5-difluoro-phenyl)-[1,2,4]oxadiazole,

3-(3-Chloromethyl-[1,2,4]oxadiazol-5-yl)-benzonitrile,

2-Chloro-4-(3-chloromethyl-[1,2,4]oxadiazol-5-yl)-pyridine,

3-Chloromethyl-5-(2,5-dimethyl-phenyl)-[1,2,4]oxadiazole ,

3-Chloromethyl-5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazole,

3-Chloromethyl-5-(2,5-dichloro-phenyl)-[1,2,4]oxadiazole,

3-Chloromethyl-5-(2-fluoro-5-bromo-phenyl)-[1,2,4]oxadiazole,

3-Chloromethyl-5-(3-methyl-phenyl)-[1,2,4]oxadiazole ,

3-Chloromethyl-5-(2,5-difluoro-phenyl)-[1,2,4]oxadiazole ,

3-Chloromethyl-5-(3-methylsulfanyl-phenyl)-[1,2,4]oxadiazole ,

3-Chloromethyl-5-(3-cyclopropyl-phenyl)-[1,2,4]oxadiazole,

3-(3-Chloromethyl-[1,2,4]oxadiazol-5-yl)-phenyl]-carbamic acid tert-butyl ester,

1-[3-(3-Chloromethyl-[1,2,4]oxadiazol-5-yl)-phenyl]-ethanone,

5-(5-Chloro-2-fluoro-phenyl)-3-chloromethyl-[1,2,4]oxadiazole,

2-(3-Chloromethyl-[1,2,4]oxadiazol-5-yl)-4-methyl-phenol,

3-Chloromethyl-5-(2-chloro-5-methyl-phenyl)-[1,2,4]oxadiazole,

3-Chloromethyl-5-(2,5-dichloro-thiophen-3-yl)-[1,2,4]oxadiazole,

3-(3-Chloromethyl-[1,2,4]oxadiazol-5-yl)-benzonitrile,

3-Chloromethyl-5-(3-fluoro-phenyl)-[1,2,4]oxadiazole ,

3-Chloromethyl-5-(2-methyl-thiazol-4-yl)-[1,2,4]oxadiazole,

3-Chloromethyl-5-(4-fluoro-phenyl)-[1,2,4]oxadiazole ,

5-(5-Bromo-2-fluoro-phenyl)-3-chloromethyl-[1,2,4]oxadiazole,

3-Chloromethyl-5-(4-methyl-thiophen-2-yl)-[1,2,4]oxadiazole,

5-(3-chloromethyl-[1,2,4]oxadiazol-5-yl)-thiophene-3-carbonitrile,

2-(3-Chloromethyl-[1,2,4]oxadiazol-5-yl)-4-methyl-benzonitrile,

3-(3-Chloromethyl-[1,2,4]oxadiazol-5-yl)-5-fluoro-benzonitrile,

3-(3-Chloromethyl-[1,2,4]oxadiazol-5-yl)-4-fluoro-benzonitrile,

4-Chloro-2-(3-chloromethyl-[1,2,4]oxadiazol-5-yl)-phenol,

3-(1-Chloro-ethyl)-5-(3-chloro-phenyl)-[1,2,4]oxadiazole,

3-(1-Chloro-ethyl)-5-(3-fluoro-phenyl)-[1,2,4]oxadiazole,

3-(1-Chloro-ethyl)-5-(5-chloro-2-fluoro-phenyl)-[1,2,4]oxadiazole,

[3-(3-Chloromethyl-[1,2,4]oxadiazol-5-yl)-phenyl]-methanol,

3-Chloromethyl-5-[1-(toluene-4-sulfonyl)-1H-pyr rol-3-yl]-[1,2,4]oxadiazole,

3-Chloromethyl-5-furan-3-yl-[1,2,4]oxadiazole,

3-Chloromethyl-5-(5-chloro-thiophen-2-yl)-[1,2,4]oxadiazole,

1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethanol,

[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-yl]-methanol,

1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethanol,

[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-methanol,

2-Chloromethyl-5-(2-fluoro-5-methyl-phenyl)-[1,3,4]oxadiazole,

2-Chloromethyl-5-(3-chloro-phenyl)-[1,3,4]oxadiazole,

4-(5-Chloromethyl-[1,3,4]oxadiazol-2-yl)-2-methyl-pyridine,

2-Chloromethyl-5-m-tolyl-[1,3,4]oxadiazole,

3-(5-Chloromethyl-[1,3,4]oxadiazol-2-yl)-benzonitrile,

2-Chloro-4-(5-chloromethyl-[1,3,4]oxadiazol-2-yl)-pyridine,

2-(5-Chloro-2-fluoro-phenyl)-5-chloromethyl-[1,3,4]oxadiazole,

2-(1-Bromo-ethyl)-5-(3-chloro-phenyl)-[1,3,4]oxadiazole,

2-(1-Bromo-ethyl)-5-(5-chloro-2-fluoro-phenyl)-[1,3,4]oxadiazole,

4-[5-(1-Bromo-ethyl)-[1,3,4]oxadiazol-2-yl]-2-methyl-pyridine,

2-(1-Bromo-ethyl)-5-(2-fluoro-5-methyl-phenyl)-[1,3,4]oxadiazole,

2-(1-Bromo-ethyl)-5-(3-chloro-phenyl)-[1,3,4]oxadiazole,

3-(1-Bromo-ethyl)-5-(3-chloro-phenyl)-[1,2,4]oxadiazole,

1-[5-(3-Chloro-phenyl)-isoxazol-3-yl]-ethanol,

1-[5-(2-Fluoro-5-methyl-phenyl)-isoxazol-3-yl]-ethanol,

5-(2-Fluoro-5-methyl-phenyl)-isoxazole-3-carboxylic acid methyl ester,

5-Thiophen-3-yl-isoxazole-3-carboxylic acid methyl ester,

5-Phenyl-isoxazole-3-carboxylic acid methyl ester,

5-(3-Chloro-phenyl)-4-methyl-isoxazole-3-carboxylic acid ethyl ester,

5-(5-Chloro-thiophen-3-yl)-isoxazole-3-carboxylic acid methyl ester,

[5-(3-Chloro-phenyl)-isoxazol-3-yl]-methanol,

[2-(3-Chloro-phenyl)-oxazol-4-yl]-methanol,

[3-(3-Chloro-phenyl)-isoxazol-5-yl]-methanol,

5-(Thiophen-3-yl-isoxazol-3-yl)methanol,

[5-(2-Fluoro-5-methyl-phenyl)-isoxazol-3-yl]-methanol,

(5-Phenyl-isoxazol-3-yl)-methanol,

[5-(3-Chloro-phenyl)-4-methyl-isoxazol-3-yl]-methanol,

[5-(5-Chloro-thiophen-3-yl)-isoxazol-3-yl)]-methanol,

Methanesulfonic acid 1-[5-(3-Chloro-phenyl)-isoxazol-3-yl]-ethyl ester,

Methanesulfonic acid 2-(3-chloro-phenyl)-oxazol-4-ylmethyl ester,
Methanesulfonic acid 3-(3-chloro-phenyl)-isoazol-5-ylmethyl ester,
Methanesulfonic acid 5-(2-fluoro-5-methyl-phenyl)-isoxazol-3-ylmethyl ester,
Methanesulfonic acid -phenyl)-isoxazol-5-yl]-ethyl ester,
Methanesulfonic acid 5-(5-chloro-2-fluoro-phenyl)-isoxazol-3-ylmethyl ester,
Methanesulfonic acid 5-(3-chloro-phenyl)-isoxazol-3-ylmethyl ester,
Methanesulfonic acid 5-thiophen-3-yl-isoxazol-3-ylmethyl ester,
Methanesulfonic acid 5-(2-fluoro-5-methyl-phenyl)-isoxazol-3-ylmethyl ester,
Methanesulfonic acid 5-phenyl-isoxazol-3-ylmethyl ester,
Methanesulfonic acid 5-(3-chloro-phenyl)-4-methyl-isoxazol-3-ylmethyl ester,
Methanesulfonic acid 5-(5-chloro-thiophen-3-yl)-isoxazol-3-ylmethyl ester,
Methanesulfonic acid 1-[5-(2-fluoro-5-methyl-phenyl)-isoxazol-3-yl]-ethyl ester,
Methanesulfonic acid 1-[5-(5-chloro-2-fluoro-phenyl)-isoxazol-3-yl]-ethyl ester,
Methanesulfonic acid 4-chloro-5-(3-chloro-phenyl)-isoxazol-3-ylmethyl ester,
Pyrimidine-4-carboxylic acid,
3-(3-Chloro-phenyl)-isoxazole-5-carboxylic acid methyl ester,
2-Bromomethyl-5-(3-chloro-phenyl)-oxazole,
2-(3-Chloro-phenyl)-oxazole-4-carboxylic acid methyl ester,
2-(3-Chloro-phenyl)-oxazole-4-carboxylic acid methyl ester,
1-[5-(5-Chloro-2-fluoro-phenyl)-isoxazol-3-yl]-ethanol,
1-[3-(3-Chloro-phenyl)-isoxazol-5-yl]-ethanol,
[5-(5-Chloro-2-fluoro-phenyl)-isoxazol-3-yl]-methanol,
3-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-propionic acid hydrazide,
3-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-butyric acid hydrazide,
3-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propionimidic acid ethyl ester hydrochloride,
3-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propionic acid hydrazide,
[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-acetic acid hydrazide,
(R)-3-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-butyric acid hydrazide,
3-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-3-methyl-butyric acid hydrazide,
3-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethyl]-piperidin-2-one,

3-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethyl]-piperidin-2-one,
3-Chloromethyl-5-(5-chloro-thiophen-3-yl)-[1,2,4]oxadiazole,
1-[5-(5-Chloro-thiophen-3-yl)-[1,2,4]oxadiazol-3-ylmethoxy]-1H-benzotriazole,
(4-Methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-acetonitrile,
2-(4-Methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-propionic acid,
2-(4-Methyl-5-pyridin-3-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-propionic acid,
3-(3-Chloro-phenyl)-5-(4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole or,
{3-[3-(4-Methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl-phenyl}-carbamic acid tert-butyl ester.

Pharmaceutical formulations

[0191] According to one aspect of the present invention there is provided a pharmaceutical formulation comprising a compound of formula I, or salt thereof, for use in the prevention and/or treatment of metabotropic glutamate receptor subtype 5 receptor (mGluR5) mediated disorders and any disorder listed below.

[0192] The composition may be in a form suitable for oral administration, for example as a tablet, pill, syrup, powder, granule or capsule, for parenteral injection (including intravenous, subcutaneous, intramuscular, intravascular or infusion) as a sterile solution, suspension or emulsion, for topical administration as an ointment, patch or cream or for rectal administration as a suppository.

[0193] In general the above compositions may be prepared in a conventional manner using one or more conventional excipients, pharmaceutical diluents and/or inert carriers.

[0194] According to another aspect of the invention thee is provided a pharmaceutical formulation comprising as active ingredient a therapeutically effective amount of a compound of formula I in association with one or more pharmaceutically acceptable diluent, excipients and/or inert carrier.

[0195] Suitable daily doses of the compounds of formula I in the treatment of a mammal, including man are approximately 0.01 to 250 mg/kg bodyweight at peroral administration and about 0.001 to 250 mg/kg bodyweight at parenteral administration.

The typical daily dose of the active ingredients varies within a wide range and will depend on various factors such as the relevant indication, the route of administration, the age, weight and sex of the patient and may be determined by a physician.

Medical use

[0196] It has been found that the compounds according to the present invention, or salts thereof, exhibit a high degree of potency and selectivity for individual metabotropic glutamate receptor (mGluR) subtypes. In particular there are compounds according to the present invention that are potent and selective for the mGluR Group I receptor and more particularly for mGluR5. Accordingly, the compounds of the present invention are expected to be useful in the prevention and/or treatment of conditions associated with excitatory activation of an mGluR Group I receptor and for inhibiting neuronal damage caused by excitatory activation of an mGluR Group I receptor, specifically when the mGluR Group I receptor is mGluR5. The compounds may be used to produce an inhibitory effect of mGluR Group I, especially mGluR5, in mammals, including man.

[0197] mGluR5 is highly expressed in the central and peripheral nervous system and in other tissues. Thus, it is expected that the compounds of the invention are well suited for the prevention and/or treatment of mGluR5 receptor-mediated disorders such as acute and chronic neurological and psychiatric disorders and chronic and acute pain disorders.

[0198] Further disorders are Alzheimer's disease, senile dementia, AIDS-induced dementia, Parkinson's disease, amyotrophic lateral sclerosis, Huntington's Chorea, migraine, epilepsy, schizophrenia, depression, anxiety, acute anxiety, obsessive compulsive disorder, ophthalmological disorders such as retinopathies, diabetic retinopathies, glaucoma, auditory neuropathic disorders such as tinnitus, chemotherapy induced neuropathies, post-herpetic neuralgia and trigeminal neuralgia, tolerance, dependency, addiction and craving disorders, neurodevelopmental disorders including Fragile X, autism, mental retardation, schizophrenia and Down's Syndrome.

[0199] The compounds are also well suited for the prevention and/or treatment of pain related to migraine, inflammatory pain, neuropathic pain disorders such as

diabetic neuropathies, arthritis and rheumatitiod diseases, low back pain, post-operative pain and pain associated with various conditions including angina, renal or billiary colic, menstruation, migraine and gout.

[0200] Other disorders are stroke, head trauma, anoxic and ischemic injuries, hypoglycemia, cardiovascular diseases and epilepsy.

[0201] The dose required for the therapeutic or preventive treatment of a particular disorder will necessarily be varied depending on the host treated, the route of administration and the severity of the illness being treated.

[0202] The invention relates to compounds of formula I as defined hereinbefore, for use in therapy.

[0203] The invention relates to compounds of formula I as defined hereinbefore, for use in prevention and/or treatment of neurological disorders.

[0204] The invention relates to compounds of formula I as defined hereinbefore, for use in prevention and/or treatment of psychiatric disorders.

[0205] The invention relates to compounds of formula I as defined hereinbefore, , for use in prevention and/or treatment of chronic and acute pain disorders.

[0206] The invention relates to compounds of formula I as defined hereinbefore, for use in prevention and/or treatment of mGluR5 receptor-mediated disorders.

[0207] The invention relates to compounds of formula I as defined hereinbefore, for use in prevention and/or treatment of Alzheimer's disease senile dementia, AIDS-induced dementia, Parkinson's disease, amylotropic lateral sclerosis, Huntington's Chorea, migraine, epilepsy, schizophrenia, depression, anxiety, acute anxiety, ophthalmological disorders such as retinopathies, diabetic retinopathies, glaucoma, auditory neuropathic disorders such as tinnitus, chemotherapy induced neuropathies, post-herpetic neuralgia and trigeminal neuralgia, tolerance, dependency, Fragile X, autism, mental retardation, schizophrenia and Down's Syndrome.

[0208] The invention relates to compounds of formula I as defined hereinbefore, for use in prevention and/or treatment of pain related to migraine, inflammatory pain, neuropathic pain disorders such as diabetic neuropathies, arthritis and rheumatitiod diseases, low back pain, post-operative pain and pain associated with various conditions including angina, renal or billiary colic, menstruation, migraine and gout.

[0209] The invention relates to compounds of formula I as defined hereinbefore, for use in prevention and/or treatment of stroke, head trauma, anoxic and ischemic injuries, hypoglycemia, cardiovascular diseases and epilepsy.

[0210] The present invention relates to the use of a compound according to Formula I and Formula II in the treatment of gastrointestinal disorders.

[0211] Another embodiment of the invention relates to the use of a compound according to Formula I and Formula II, for the manufacture of a medicament for the inhibition of transient lower esophageal sphincter relaxations, for the treatment of GERD, for the prevention of G.I. reflux, for the treatment regurgitation, treatment of asthma, treatment of laryngitis, treatment of lung disease and for the management of failure to thrive.

[0212] The present invention relates also to the use of a compound of formula I as defined hereinbefore, in the manufacture of a medicament for the prevention and/or treatment of mGluR5 receptor-mediated disorders and any disorder listed above.

[0213] The invention also provides a method of treatment and/or prevention of mGluR5 receptor-mediated disorders and any disorder listed above, in a patient suffering from, or at risk of, said condition, which comprises administering to the patient an effective amount of a compound of formula I, as hereinbefore defined.

[0214] In the context of the present specification, the term "therapy" includes treatment as well as prevention, unless there are specific indications to the contrary. The terms "therapeutic" and "therapeutically" should be construed accordingly.

[0215] In this specification, unless stated otherwise, the term 'antagonist' means a compound that by any means, partly or completely, blocks the transduction pathway leading to the production of a response by the ligand.

[0216] The term "disorder", unless stated otherwise, means any condition and disease associated with metabotropic glutamate receptor activity.

Non- Medical use

[0217] In addition to their use in therapeutic medicine, the compounds of formula I or salt thereof, are also useful as pharmacological tools in the development and standardisation of *in vitro* and *in vivo* test systems for the evaluation of the effects of

inhibitors of mGluR related activity in laboratory animals such as cats, dogs, rabbits, monkeys, rats and mice, as part of the search for new therapeutics agents.

Pharmacology

[0218] The pharmacological properties of the compounds of the invention can be analyzed using standard assays for functional activity. Examples of glutamate receptor assays are well known in the art as described in for example Aramori *et al., Neuron* 8:757 (1992), Tanabe *et* al., *Neuron* 8:169 (1992), Miller *et al., J. Neuroscience* 15: 6103 (1995), Balazs, *et al., J. Neurochemistry* 69:151 (1997). The methodology described in these publications is incorporated herein by reference. Conveniently, the compounds of the invention can be studied by means of an assay that measures the mobilization of intracellular calcium, $[Ca^{2+}]_i$ in cells expressing mGluR5.

[0219] Intracellular calcium mobilization was measured by detecting changes in fluorescence of cells loaded with the fluorescent indicator fluo-3. Fluorescent signals were measured using the FLIPR system (Molecular Devices). A two addition experiment was used that could detect compounds that either activate or antagonize the receptor.

[0220] For FLIPR analysis, cells expressing human mGluR5d were seeded on collagen coated clear bottom 96-well plates with black sides and analysis of $[Ca^{2+}]_i$ mobilization was done 24 hours after seeding.

[0221] FLIPR experiments were done using a laser setting of 0.800 W and a 0.4 second CCD camera shutter speed. Each FLIPR experiment was initiated with 160 μL of buffer present in each well of the cell plate. After each addition of the compound, the fluorescence signal was sampled 50 times at 1 second intervals followed by 3 samples at 5 second intervals. Responses were measured as the peak height of the response within the sample period.

[0222] EC_{50} and IC_{50} determinations were made from data obtained from 8-point concentration response curves (CRC) performed in duplicate. Agonist CRC were generated by scaling all responses to the maximal response observed for the plate. Antagonist block of the agonist challenge was normalized to the average response of

the agonist challenge in 14 control wells on the same plate.

[0223] We have validated a secondary functional assay for mGluR5d based on Inositol Phosphate (IP_3) turnover. IP_3 accumulation is measured as an index of receptor mediated phospholipase C turnover. GHEK cells stably expressing the human mGluR5d receptors were incubated with [3H] myo-inositol overnight, washed three times in HEPES buffered saline and pre-incubated for 10 minutes with 10 mM LiCl. Compounds (agonists) were added and incubated for 30 minutes at 37°C. Antagonist activity was determined by pre-incubating test compounds for 15 minutes, then incubating in the presence of glutamate (80μM) or DHPG (30 μM) for 30 minutes. Reactions were terminated by the addition of perchloric acid (5%). Samples were collected and neutralized, and inositol phosphates were separated using Gravity-Fed Ion-Exchange Columns.

[0224] A detailed protocol for testing the compounds of the invention is provided below in Pharmaceutical Examples.

[0225] Abbreviations

FLIPR	Fluorometric Imaging Plate reader
CCD	Charge Coupled Device
CRC	Concentration Response Curve
GHEK	Human Embrionic Kidney expressing Glutamate Transporter
HEPES	4-(2-hydroxyethyl)-1-piperazineethanesulfonic acid (buffer)
IP_3	inositol triphosphate
DHPG	3,5-dihydroxyphenylglycine;
BSA	Bovine Serum Albumin
EDTA	Ethylene Diamine Tetraacetic Acid

Methods of Preparation

[0226] Another aspect of the present invention provides a process for preparing a compound of formula **I**, or salt thereof.

[0227] Throughout the following description of such processes it is understood that, where appropriate, suitable protecting groups will be added to, and subsequently removed from, the various reactants and intermediates in a manner that will be readily

understood by one skilled in the art of organic synthesis. Conventional procedures for using such protecting groups as well as examples of suitable protecting groups are described, for example, in "Protective Groups in Organic Synthesis" T.W. Green, P.G.M. Wuts, Wiley-Interscience, New York, 1999. It is also to be understood that a transformation of a group or substituent into another group or substituent by chemical manipulation can be conducted on any intermediate or final product on the synthetic path toward the final product, in which the possible type of transformation is limited only by inherent incompatibility of other functionalities carried by the molecule at that stage to the conditions or reagents employed in the transformation. Such inherent incompatibilities, and ways to circumvent them by carrying out appropriate transformations and synthetic steps in a suitable order, will be readily understood to the one skilled in the art of organic synthesis. Examples of transformations are given below, and it is to be understood that the described transformations are not limited only to the generic groups or substituents for which the transformations are exemplified. References and descriptions on other suitable transformations are given in "Comprehensive Organic Transformations – A Guide to Functional Group Preparations" R. C. Larock, VHC Publishers, Inc. (1989). References and descriptions of other suitable reactions are described in textbooks of organic chemistry, for example, "Advanced Organic Chemistry", March, 4th ed. McGraw Hill (1992) or, "Organic Synthesis", Smith, McGraw Hill, (1994). Techniques for purification of intermediates and final products include for example, straight and reversed phase chromatography on column or rotating plate, recrystallisation, distillation and liquid-liquid or solid-liquid extraction, which will be readily understood by the one skilled in the art. The definitions of substituents and groups are as in formula I except where defined differently. The term "room temperature" and "ambient temperature" shall mean, unless otherwise specified, a temperature between 16 and 25 °C.

[0228] Unless specified otherwise, are P, Q, X^1, X^2, X^3, X^4, R, R^1, R^2, R^3, R^4, R^5, R^6, M^1, M^2, m and n, defined as in formula I.

[0229] All starting materials are commercially available or earlier described in the literature.

[0230] The ^{1}H and ^{13}C NMR spectra were recorded either on Bruker 300, Bruker DPX400 or Varian +400 spectrometers operating at 300, 400 and 400 MHz for ^{1}H NMR respectively, using TMS or the residual solvent signal as reference, in deuterated chloroform as solvent unless otherwise indicated. All reported chemical shifts are in ppm on the delta-scale, and the fine splitting of the signals as appearing in the recordings (s: singlet, d: doublet, t: triplet, q: quartet, m: multiplet).

[0231] Analytical in line liquid chromatography separations followed by mass spectra detections, were recorded on a Waters LCMS consisting of an Alliance 2795 (LC) and a ZQ single quadropole mass spectrometer. The mass spectrometer was equipped with an electrospray ion source operated in a positive or negative ion mode. The ion spray voltage was ±3 kV and the mass spectrometer was scanned from *m/z* 100-700 at a scan time of 0.8 s. To the column, X-Terra MS, Waters, C8, 2.1 x 50mm, 3.5 μm, was applied a linear gradient from 5 % to 100% acetonitrile in10 mM ammonium acetate (aq.), or in 0.1% TFA (aq.).

[0232] Preparative reversed phase chromatography was run on a Gilson autopreparative HPLC with a diode array detector using an XTerra MS C8, 19x300mm, 7μm as column.

[0233] MS-triggered preparative reversed phase chromatograpy was run on a Waters autopurification LC-MS system with a diode array detector and a ZQ mass detector using an XTerra MS C8, 19x100 mm, 5 μm as column.

[0234] Purification by a chromatotron was performed on rotating silica gel / gypsum (Merck, 60 PF-254 with calcium sulphate) coated glass sheets, with coating layer of 1, 2, or 4 mm using a TC Research 7924T chromatotron.

[0235] Purification of products were also done using Chem Elut Extraction Columns (Varian, cat #1219-8002), Mega BE-SI (Bond Elut Silica) SPE Columns (Varian, cat # 12256018; 12256026; 12256034), or by flash chromatography in silica-filled glass columns.

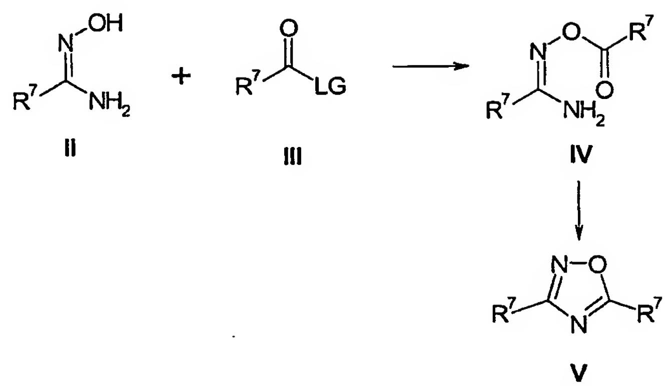
[0236] Microwave heating was performed in a Smith Synthesizer Single-mode microwave cavity producing continuous irradiation at 2450 MHz (Personal Chemistry AB, Uppsala, Sweden).

[0237] Abbreviations:

atm	atmosphere
aq.	aqueous
CDI	N,N'-Carbonyldiimidazole
d	day(s)
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
DCC	N,N-Dicyclohexylcarbodiimide
DCM	Dichloromethane
DEA	N,N-Diisopropyl ethylamine
DIC	N,N'-Diisopropylcarbodiimide
DMAP	N,N-Dimethyl-4-aminopyridine
DMF	*N,N*-dimethylformamide
DMSO	Dimethylsulfoxide
EA	Ethyl acetate
BOPA	Benzoyl Peroxide
EDCl	N-[3-(dimethylamino)propyl]-N'-ethylcarbodiimide hydrochloride
EtOH	Ethanol
Et_2O	Diethylether
h	hour(s)
hep	heptane
hex	hexane(s)
P-BEMP	Polystyrene bound 2-tert-Butylimino-2-diethylamino-1,3-dimethyl-perhydro-1,3,2-diazaphosporine
Deoxofluor	[Bis(2-methoxyethyl)amino]sulfur trifluoride
DAST	(Diethylamino)sulfur trifluoride
EDCI	1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride
HOBt	1-hydroxybenzotriazole hydrate
THF	tetrahydrofuran
TFA	trifluoroacetic acid
Et	ethyl
Ac	acetyl
DIBAL	diisobutylaluminum hydride

M, N	molar and normal
MeOH	Methanol
HBTU	*O*-Benzotriazol-1-yl-*N,N,N',N'*-tetramethyluronium hexafluorophosphate
Boc	tert-butoxycarbonyloxy
HMDS	hexamethyl disilazide
Ms	mesylate or methanesulphonyl
min	minutes
NADPH	Nicotinamide-adenine dinucleotide phosphate, reduced
nBuLi	1-butyl lithium
NBS	N-bromosuccinimid
Novozyme 435®	Trademark name for polymer supported *Candida Antartica Lipase*
o.n.	over night
prep	preparative
r.t. or rt	room temperature
sat.	saturated
TEA	Triethylamine
LDA	Lithium diisopropylamine
LHA	Lithium aluminium hydride
MCPBA	meta-chloroperoxybenzoic acid
SPE	solid phase extraction
Lawesson's Reagent	[2,4-bis(4-methoxyphenyl)-1,3-dithia-2,4-diphosphetane-2,4-disulfide
TFA	Trifluoroacetic acid
Ts	tosyl or *para*-toluene sulphonyl

[0238] General syntheses of compounds of formula V.



[0239] A compound of formula V, wherein R^7 is independently selected from a group consisting of M^1-$(R^2)_n$-P-$(R^1)_{m1}$, M^2-$(R^3)_n$-X^4-Q-$(R^4)_{m2}$, and M^2-$(R^3)_n$-G wherein G is a leaving group or a group which may subsequently be transformed into a leaving group, may be prepared through cyclization of a compound of formula **IV** formed from a suitably activated compound of formula **III**, wherein LG is a leaving group, with a compound of formula **II**. The compound of formula **II** may be prepared from a suitable nitrile by addition of hydroxylamine in a suitable solvent such as, methanol, ethanol, water or mixture thereof, using an appropriate base such as hydroxide, carbonate or acetate.

[0240] The compound of formula **III** may be activated as follows; i) as the acid chloride formed from the acid using a suitable reagent such as oxalyl chloride or thionyl chloride; ii) as an anhydride or mixed anhydride formed from treatment with a reagent such as alkyl chloroformate; iii) using traditional methods to activate acids in amide coupling reactions such as EDCI with HOBt or uronium salts like HBTU; iv) as an alkyl ester when the hydroxyamidine is deprotonated using a strong base like tert-butoxide; v) by any other suitable method of activation for the desired substrate.

[0241] The ester formation may be accomplished using an appropriate aprotic solvent such as dichloromethane, tetrahydrofuran, *N,N*-dimethylformamide or toluene, with optionally an appropriate organic base such as triethylamine, diisopropylethylamine and the like or an inorganic base such sodium bicarbonate or potassium carbonate.

[0242] The cyclization of the ester to form an oxadiazole may be carried out on the

crude ester, with evaporation and replacement of the solvent with a higher boiling solvent such as DMF, or with aqueous extraction to provide a semi-purified material or with material purified by standard chromatographic methods. The cyclization may be accomplished by heating conventionally or by microwave irradiation (100-180°C), in a suitable solvent such as pyridine or *N,N*-dimethylformamide or using a lower temperature method employing reagents like tetrabutylammonium fluoride in tetrahydrofuran or by any other suitable known literature method.

[0243] Other compatible non-reacting functional groups suitably protected may also be present in the substrates.

[0244] Further examples of the above described reactions can be found in Poulain et al., Tetrahedron Lett., (2001), *42*, 1495-98, Ganglott et al., Tetrahedron Lett., (2001), *42*, 1441-43, which are hereby included as references.

[0245] Synthesis of Nitriles and Acids for use in preparation of compounds of formula II and III

[0246] Aryl nitriles are available by a variety of methods including cyanation of an aryl halide or triflate under palladium or nickel catalysis using an appropriate cyanide source such as zinc cyanide in an appropriate solvent such as *N,N*-dimethylformamide. The corresponding acid is available from the nitrile by hydrolysis under either acidic or basic conditions in an appropriate solvent such as aqueous alcohols. Aryl acids are also available from a variety of other sources, including iodo- or bromo- lithium exchange followed by trapping with CO_2 to give directly the acid.

[0247] The acid may be converted to the primary amide using any compatible method to activate the acid, including via the acid chloride or mixed anhydride, followed by trapping with any source of ammonia, including ammonium chloride in the presence of a suitable base, ammonium hydroxide, methanolic ammonia or ammonia in an aprotic solvent such as dioxane. This amide intermediate may be converted to the nitrile using a variety of dehydration reagents such as oxalyl chloride or thionyl chloride. This reaction sequence to convert an acid into a nitrile may also be applied to non-aromatic acids, including suitably protected amino acid derivatives.

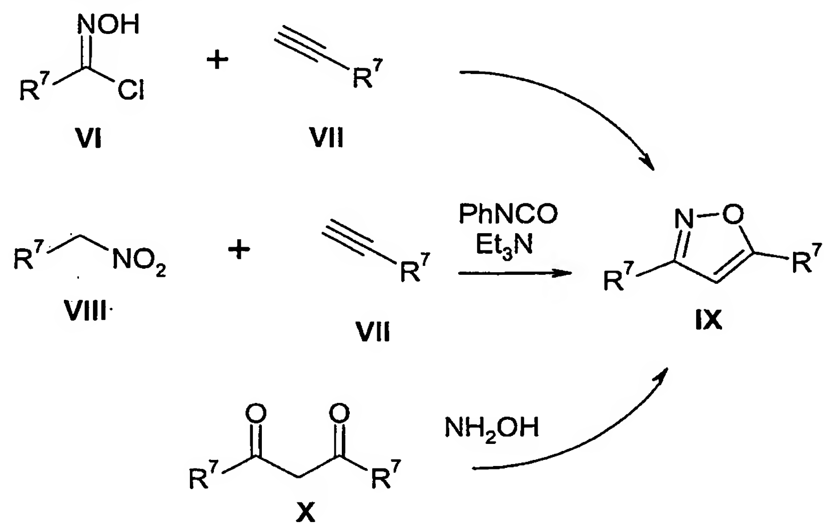
A suitable protecting group for an amine, in an amino acid or in a remote position of any other acid starting material, may be any group which removes the basicity and nucleophilicity of the amine functionality, including such carbamate protecting group as Boc.

[0248] Some acids are more easily prepared taking advantage of commercially available analogs. For example, 6-methylpyridine-4-carboxylic acid is prepared by dechlorination of 2-chloro-6-methylpyridine-4-carboxylic acid. Certain types of substituted fluoro-benzonitriles and benzoic acids are available from bromo-difluoro-benzene via displacement of one fluoro group with a suitable nucleophile such as imidazole in the presence of a base such as potassium carbonate in a compatible solvent such as *N,N*-dimethylformamide at elevated temperatures (80-120°C) for extended periods of time. The bromo group may subsequently be elaborated into the acid or nitrile as above.

[0249] 1,3-Disubsituted and 1,3,5-trisubstituted benzoic acids and benzonitriles may be prepared by taking advantage of readily available substituted isophthalic acid derivatives. Monohydrolysis of the diester allows selective reaction of the acid with a variety of reagents, most typically activating agents such as thionyl chloride, oxalyl chloride or isobutyl chloroformate and the like. From the activated acid, a number of products are available. In addition to the primary amide used to form the nitrile by dehydration as mentioned above, reduction to the hydroxymethyl analog may be carried out on the mixed anhydride or acid chloride using a variety of reducing agents such as sodium borohydride in a compatible solvent such as tetrahydrofuran. The hydroxymethyl derivative may be further reduced to the methyl analog using catalytic hydrogenation with an appropriate source of catalyst such as palladium on carbon in an appropriate solvent such as ethanol. The hydroxymethyl group may also be used in any reaction suitable for benzylic alcohols such as acylation, alkylation, transformation to halogen and the like. Halomethylbenzoic acids of this type may also be obtained from bromination of the methyl derivative when not commercially available. Ethers obtained by alkylation of the hydroxymethyl derivatives may also be obtained from the halomethylaryl benzoate derivatives by reaction with the appropriate alcohol using an appropriate base such as potassium carbonate or sodium

hydroxide in an appropriate solvent such as tetrahydrofuran or the alcohol. When other substituents are present, these may also be employed in standard transformation reactions. Treatment of an aniline with acid and sodium nitrite may yield a diazonium salt, which may be transformed into a halide such as fluoride using tetrafluoroboric acid. Phenols react in the presence of a suitable base such as potassium carbonate with alkylating agents to form aromatic ethers.

[0250] Formation of compounds of formula IX



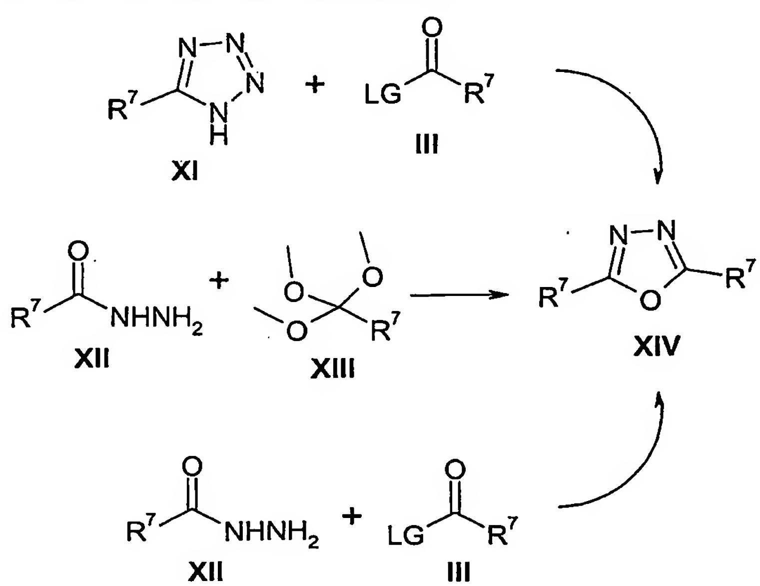
[0251] A compound of formula **IX**, wherein R^7 is independently selected from a group consisting of M^1-$(R^2)_n$-P-$(R^1)_{m1}$, M^2-$(R^3)_n$-X^4-Q-$(R^4)_{m2}$, and M^2-$(R^3)_n$-G wherein G is a leaving group or a group which may subsequently be transformed into a leaving group, may be prepared by a 1,3-dipolar cycloaddition between compounds of formula **VI** and **VII** under basic conditions using a suitable base such as sodium bicarbonate or triethylamine at suitable temperatures (0°C – 100°C) in solvents such as toluene. Synthesis of compounds of type **VI** has previously been described in the literature, e.g. Kim, Jae Nyoung; Ryu, Eung K; J. Org. Chem. (1992), 57, 6649-50. 1,3-Dipolar cycloaddition with acetylenes of type **VII** can also be effected using substituted nitromethanes of type **VIII** via activation with an electrophilic reagent such as PhNCO in the presence of a base such as triethylamine at elevated

temperatures (50-100 °C). Li, C-S.; Lacasse, E.; Tetrahedron Lett. (2002) *43*; 3565 - 3568. Several compounds of type **VII** are commercially available, or may be synthesized by standard methods as known by one skilled in the art.

[0252] Alternativley, compounds of formula **X**, which are available from a Claisen condensation of a methyl keone and an ester using basic conditions using such bases as sodium hydride or potassium tert-butoxide, may yield compounds of formula **IX** via condensation and subsequent cyclization using hydroxylamine, for example in the form of the hydrochloric acid salt, at elevated temperatures (60-120°C).

[0253] It is understood that for both methods subsequent functional group transformations may be necessary. In the case of an ester group, these transformations may include, but is not limited to either of following three procedures: a) Complete reduction using a suitable reducing agent such as LAH in solvents such as THF. b) Partial reduction using a suitable selective reducing agent such as DIBAL followed by alkylation with an alkylhalide. c) Alkylation using an alkylmetal reagent such as an alkyl magnesium halide in solvents such as toluene or THF, followed by reduction with for example sodium borohydride in methanol.

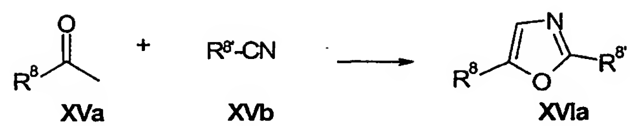
[0254] Formation of compounds of formula XIV

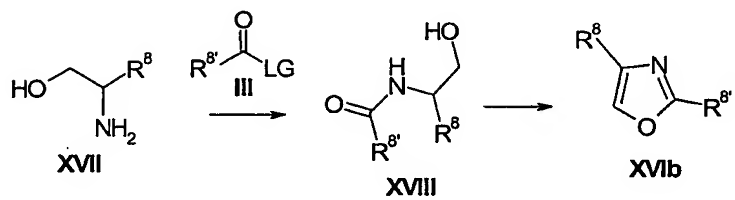


[0255] A compound of formula **XIV**, wherein R^7 is independently selected from a group consisting of M^1-$(R^2)_n$-P-$(R^1)_{m1}$, M^2-$(R^3)_n$-X^4-Q-$(R^4)_{m2}$, and M^2-$(R^3)_n$-G wherein G is a leaving group or a group which may subsequently be transformed into a leaving group, may be prepared from tetrazole compounds of type **XI** via acylation using an isolable compound of type **III** such as an acid chloride or anhydride, or a compound of type **III** wherein the LG may be formed *in situ*, for example from activation of an acid using a reagent such as DCC or EDCI, followed by rearrangement to the 1,3,4-oxadizaole. Jursic, B.S.; Zdravkovski, Z.; Synth.Commun.; (1994) *24*; 1575-1582.

[0256] Alternatively, compounds of formula **XIV** may also be prepared from acyl hydrazide of type **XII** via heating in the presence of compounds of formula **XIII** or **III,** wherein LG is a leaving group such as chloride or alkoxide, at elevated temperatures (60-130°C) in one step. The reaction of compounds of Formula **XIII** may be carried out neat or using a suitable aprotic solvent such as benzene or xylene, or a protic solvent such as ethanol or n-butanol, and may be facilitated by the presence of abase such as KOtBu or a acid such as p-toluene sulfonic acid or acetic acid. Se references: Saunders, J.; Cassidy, M.; Freedman, S. B.; Harley, E. A.; Iversen, L.L. J.Med.Chem.; (1990) 33; 1128-1138; Peet, N. P.; Sunder, S. J.Heterocycl.Chem.; (1984) 21; 1807-1816. For compounds of formula **III** a dehydrating agent such as phosphorous pentoxide may be used to increase cyclization of the formed reaction intermediate as has been previously been decribed for example by Kakefuda, Akio; et al.; Bioorg. Med. Chem. (2002), *10*; 1905-1912.

[0257] Formation of compounds of formula XVI

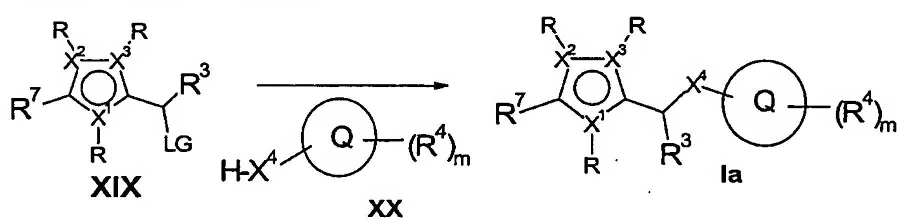




[0258] A compound of formula **XVI**, wherein R^8 as defined above is independently selected from a group consisting of M^1-$(R^2)_n$-P-$(R^1)_{m1}$, M^2-$(R^3)_n$-X^4-Q-$(R^4)_{m2}$, and M^2-$(R^3)_n$-G wherein G is a leaving group or a group which may subsequently be transformed into a leaving group, may be prepared by the reaction of compounds of formula **XVa** and **XVb** in the presence of in situ generated Tl(OTf)3 under acidic conditions according to the procedure of Lee and Hong; Tetrahedron Lett., (1997), *38*, 8959-60.

[0259] Alternatively compounds of formula **III** and **XVII** are reacted as described above for formula **V** to give an intermediate of formula **XVIII**. Such an intermediate may give the required oxazole by cyclodehydration with to generate the oxazoline followed by dehydrogenation using $BrCCl_3$ in the same reaction pot. Phillips, A.J.; Uto, Y.; Wipf, P.; Reno, M.J. and Williams, D.R., Organic Letters, (2000) *2*, 1165-8.

[0260] Formation of the bond between X^4 and M^2 or Q and M^2 through nucleophilic displacement of a leaving group:



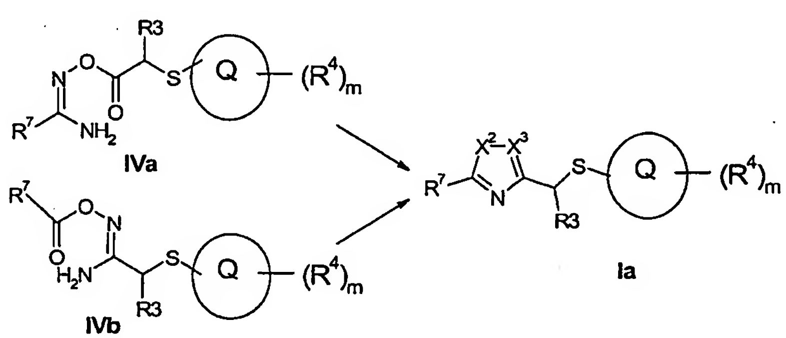
[0261] A compound of formula **XX**, may be used to displace the leaving group LG in compounds of formula **XIX** (R^7 is M^1-$(R^2)_n$-P-$(R^1)_{m1}$). When X^4 is represented by

a heteroatom such as N and S, the reaction is carried out in the presence of an appropriate base such as potassium carbonate, cesium carbonate, sodium hydride, triethylamine or the like, which may facilitate the reaction by deprotonation of the X^4 residue and prevent the formation of any excess acid that would be generated by the reaction in the absence of a base. The reaction may be accomplished using any appropriate solvent such as acetonitrile or DMF, and may be carried out at room temperature or at elevated temperature (35-100°C) to accelerate the reaction.

[0262] Such conditions may be used with appropriate modifications of employed equipment for parallel synthesis, using standard techniques known to the one skilled in the art.

[0263] Similarly these reaction conditions may be carried out for compounds of formula **XX** when X^4 = bond and ring Q is a fused bicycle containing a heteroatom such as N as defined aboved. In either the latter or the above described case with X^4=N, NaH in DMF is preferred as desribed in literature precedences, for example Murdoch, Robert; Tully, W. Roger; Westwood, Robert; J.Heterocycl.Chem.; (1986), *23*; 833-841.

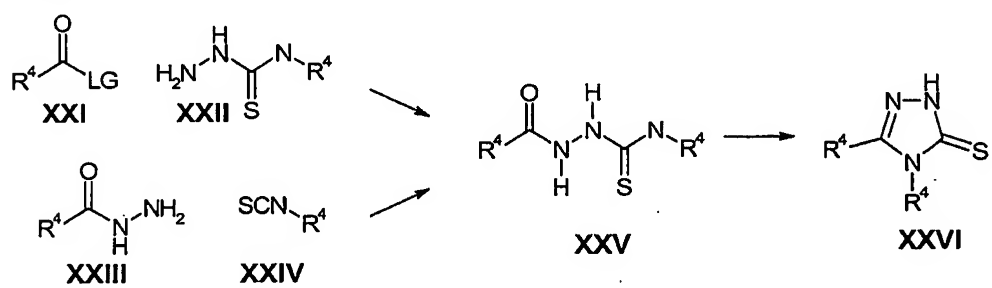
[0264] For compounds of formula **XX** containing X^4 = C a stronger base needs to be employed to achieve deprotonation, such as for example LDA, n-butyllithium or any other alkyl metal base in apropriate aprotic solvents such as THF, hexane or toluene at temperatures generally below ambient temperatures, e.g.at –78°C or 0°C.



[0265] An alternative procedure for the synthesis of above described type of thiomethyl oxadiazole is to form an acyclic ester **IVa** and **IVb** from the combination

of a suitably substituted hydroxyamidine and activated acid coupling partner also suitably substituted. Displacement of the chloride using the thiol nucleophile may occur immediately prior to cyclization using one of the methods of oxadiazole formation described above. The displacement can also be carried out on the chloromethyl hydroxyamidine or chloromethyl acid starting materials followed by the two step esterification and cyclization as above. The conditions described may be used with appropriate modifications of employed equipment for parallel synthesis using standard techniques known to the one skilled in the art.

[0266] Formation of 4-alkyl-triazoles thiols/thiones:

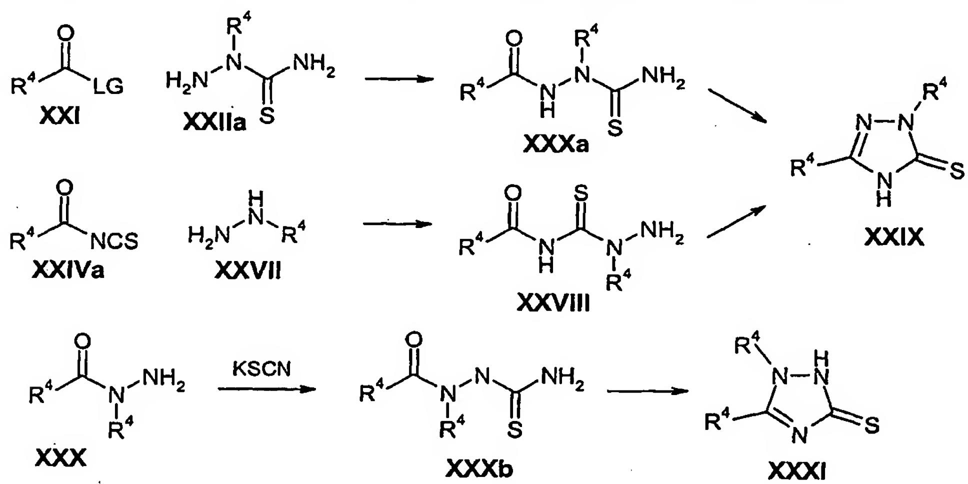


[0267] Any suitable acylating agent such as an acid chloride or an activated acid or the corresponding acid under amide coupling conditions as mentioned above, is reacted with a suitable 4-alkyl-3-thiosemicarbazide in the presence of a base such as pyridine or non-nucleophilic amines to form the acyclic intermediate compound of formula **XXV**, wherein R^4 is as defined above. The same intermediate is also available through reaction of an acyl hydrazide with an alkyl isothiocyanate. Cyclization to give a compound of formula **XXVI** is easily effected by treatment with an appropriate inorganic base such as hydroxide or bicarbonate at elevated temperature in an appropriate solvent such as water, water-dioxane, an aqueous alcohol or mixture thereof.

[0268] Such conditions may be used with appropriate modifications of employed equipment when using a solid phase base instead of above-mentioned ones, such as for example P-BEMP for parallel synthesis using standard techniques known to the one skilled in the art.

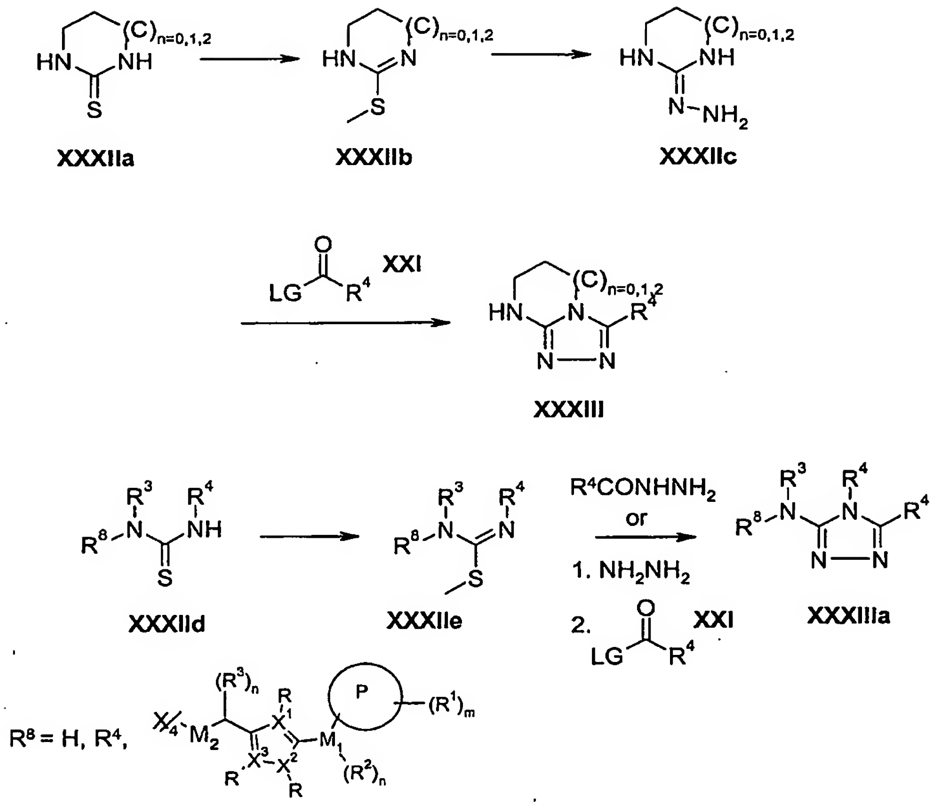
[0269] The compound of formula **XXV** reacts through its tautomeric form under the conditions described above with compounds of formula **XIX** to yield the S-alkylation compounds of the formula **Ia**.

[0270] The triazole thiones **XXIX** and **XXXI** alkylated on the other nitrogen atoms of the ring (1 and 2) are available through similar procedures. The 2-alkyl triazole thione **XXVIII** may be obtained by treatment of an aroyl isothiocyanate with an alkyl hydrazine in toluene at elevated temperatures, e.g. 85°C, followed by heating with aqueous bicarbonate. The same product may also be obtained through treatment of the analogous 2-alkyl-3-thiosemicarbazide with an activated acid in the presence of a suitable base such as pyridine or triethylamine followed by alkaline ring closure in a manner similar to the alkaline ring closure yielding product **XXVI** above.



[0271] The 1-alkyl triazole thiones **XXXI** may be prepared by the reaction of a suitable *N*-alkyl-*N*-acylhydrazide with potassium thiocyanate in the presence of an acid such as HCl or other compatible strong acid via the 1-acyl-1-alkyl-3-thiosemicarbazide intermediate which undergoes alkaline ring closure in a manner similar to the alkaline ring closure yielding compounds of formula **XXVI** above.

[0272] Formation of compounds of formula XXXIII

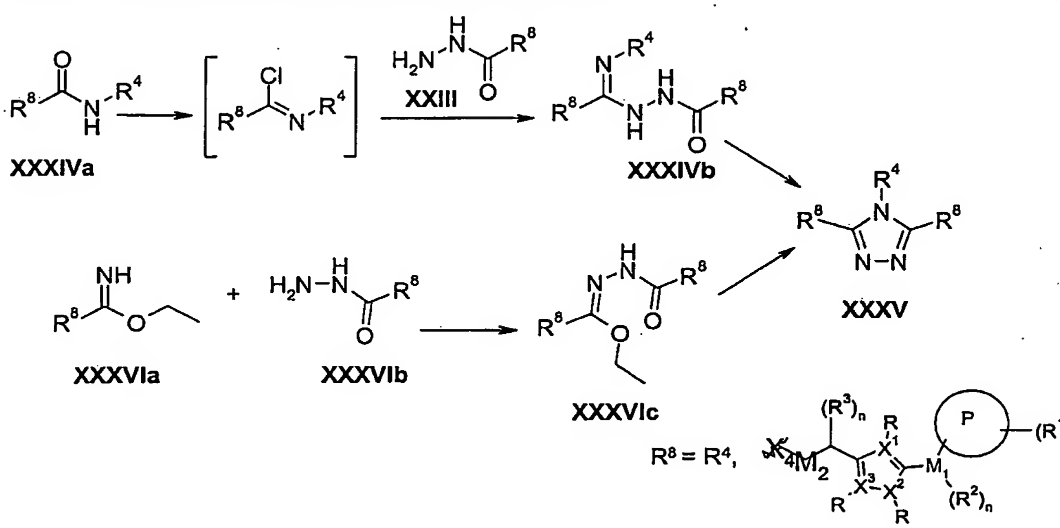


[0273] A compound of formula **XXXIII** may be prepared by alkylation of cyclic thioureas of formula **XXXIIa**, wherein n is defined as 0,1 or 2, resulting in compound of formula **XXXIIb**, e.g. 2-methylthio-1,4,5,6-tetrahydropyrimidine in case of n=1. The alkylation with for example methyliodide as alkylating agent can be done in several solvents (DMF, acetone, CH_2Cl_2 etc.) at room temperature or elevated temperatures and will give the product as its hydroiodide salt as has been previously described by Kennedy, Kevin J.; Simandan, Tiberiu L.; Dix, Thomas A.; Synth.Commun.; (1998); *24*; 741-746. Cyclic thioureas are readily available either through synthesis as known by the one skilled in the art, or commercial sources. Compounds of formula **XXXIIc** result from the hydrazinolysis of the corresponding compounds of type **XXXIIb**. The hydrazinolysis is preferably done in refluxing EtOH with hydrazine hydrate as described previously by Krezel, Izabella; Pharmazie;

(1994); *94*, 27-31. Finally, fused triazoles of formula **XXXIII** may be formed through the thermal acylation and condensation reaction between compounds of formula **XXI** wherein LG is a leaving group as for example a halide, and compounds of formula **XXXIIc** . Such reactions may be conducted in pyridine or in EtOH or toluene in the presence of base. Normal heating or microwave irradiation may be used. Similarly, **XXXIII** may be prepared in the presence of a base, such as sodium methoxide in a suitable solvent such as methanol or ethanol at elevated temperatures where **XXI** may also be an ester or carboxylic acid.

[0274] Acyclic thioureas of formula **XXXIId** , wherein R^8 is defined as in the scheme and R^3 and R^4 are as defined in Formula I, may also be employed using a similar method to obtain compounds of formula **XXXIIIa**, wherein the introduction of the hydrazine portion may be carried out using either hydrazine followed by acylation, or by using a preformed acyl hydrazine.

[0275] Formation of compounds of formula XXXV

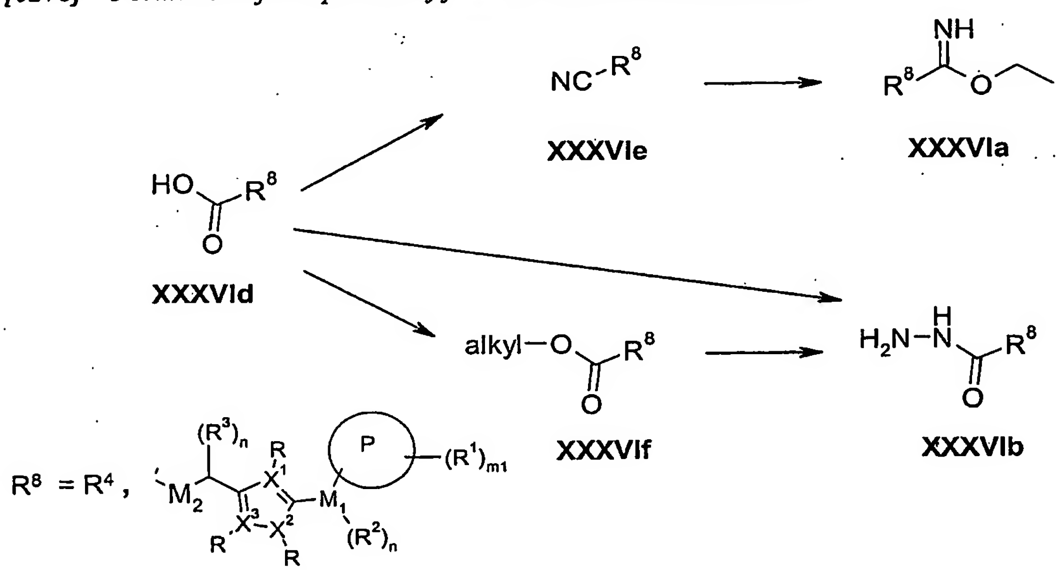


[0276] Compounds of formula **XXXIVb** may be prepared by using similar methods as above, e.g. by activation of **XXXIVa** to give the corresponding imidoyl chloride by using oxalyl chloride or pentachlorophosphine in the optional presence of a base such

as triethylamine. The intermediate may be used in-situ or may be isolated prior to trapping by a compound of formula **XXIII** as has been used above. The subsequent product may be cyclized under acidic or basic conditions in a suitable solvent such as DMF to give compounds of formula **XXXV**. **XXXV** may be an intermediate used in the formation of compounds of Formula **I**, or may be the final bioactive compound of Formula **I**.

[0277] A compound of formula **XXXV**, wherein R^8 is selected independently from a group as depicted above may also be prepared through reaction of compounds of formula **XXXVIa** (ethyl imidoate is depicted as example) and **XXXVIb** followed by cyclization at elevated temperatures (40 – 80°C) in the presence of an amine , whereas the amine preferably should have, but is not limited to, a low boiling point such as that it can be used in excess and simplify the work-up procedure. Examples for such amines may be, but are not limited to methylamine or ethylamine which may be used as solutions in for example methanol, THF or dichloromethane.

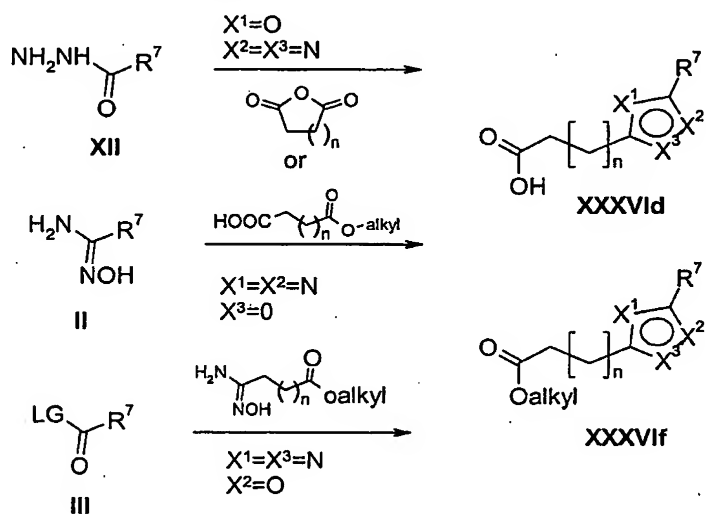
*[0278] Formation of compounds of formula **XXXVIa** and **XXXVIb***



[0279] A compound of formula **XXXVIa**, wherein R^8 is selected independently from a group as depicted above may be prepared through reaction of a nitrile of

formula **XXXVIe** in an alcohol such as ethanol in the presence of a protic acid, for example hydrochloric acid. The nitrile may be obtained from an acid **XXXVId** as described above. Compounds of formula **XXXVId** may also be used to prepare acyl hydrazides of formula **XXXVIb**, wherein R^8 is selected independently from a group as depicted above. This type of substance **XXXVIb** may also be formed directly from an acid. There may be advantages to react an intermediate ester of type **XXXVIf** with either neat hydrazine, hydrazine salt in the presence of a base or hydrazine hydrate in facilitating a simpler workup. However, the direct route via the acid using in situ activation may be advantageous in substrates sensitive to nucleophilic attack and also give the product in a shorter sequence of steps.

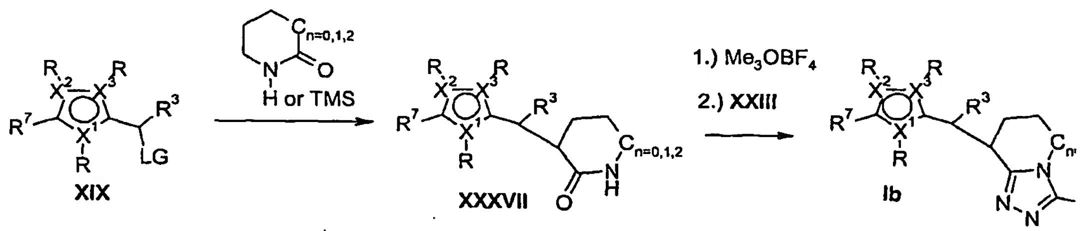
[0280] Formation of compounds of formula XXXVId and XXXVIf



[0281] Compound of formula **XXXVId & XXXVIf**, wherein R^7 is a group consisting of M^1-$(R^2)_n$-P-$(R^1)_m$, may be prepared by either of the non-limiting methods: a) reaction of acyl hydrazide compounds of formula **XII** with a cyclic anhydride or monoesterified diacid followed by the cyclization of the formed intermediate would lead to 1,3,4-oxadiazoles of type **XXXVId** and **XXXVIf** respectively (X^1=O, X^2 and X^3=N); b) reaction and cyclization of an hydroxyamidine of Formula **II** with a cyclic anhydride or with the monoesterified diacid may be used

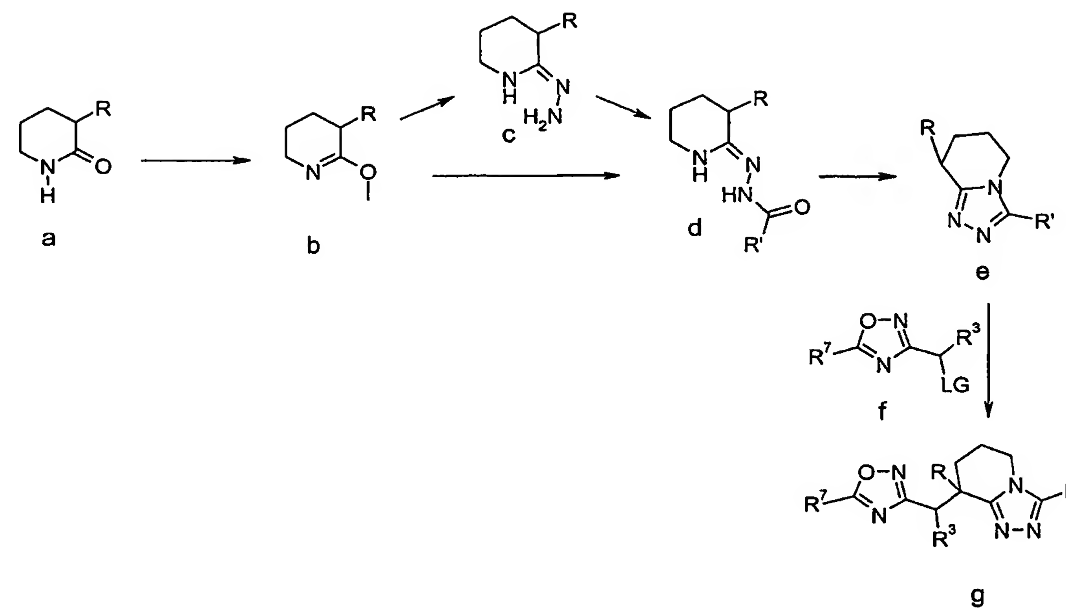
to provide the 1,2,4-oxaziazole analogs **XXXVId** and **XXXVIf** wherein X^1 and X^2 =N, X^3=O; c) reaction of a compound of type **III** with an hydroxamidine type compound, with the exception of the succinyl derivative, may be used to provide the 1,2,4-oxaziazole analogs **XXXVIf** wherein X^1 and X^3 =N, X^2=O.
Compounds **XXXVId** and **XXXVIf** may be interconverted independent of the nature of X^1, X^2 or X^3 as described above.

[0282] Formation of compounds of formula Ib



[0283] A compound of formula **Ib**, wherein R^7 is selected from a group M^1-$(R^2)_n$-P-$(R^1)_{m1}$ may be prepared from compounds of formula **XXXVII,** generated from **XIV** as described below, through selective O alkylation using Me_3OBF_4 or dimethyl sulfate (as described in literature precedences, for example: a) Sheu, Jennline; Smith, Michael B.; Oeschger, Thomas R.; Satchell, Jacqueline; Org.Prep.Proced.Int.; (1992); *24*, 147 – 158; or b) Hutchinson, Ian S.; Matlin, Stephen A.; Mete, Antonio, Tetrahedron Lett.; (2001); *42*; 1773 – 1776). The methoxy group may then be displaced by an acyl hydrazide of type **XXIII,** followed by a ring closing condensation to form the triazole heterocycle. This may be done in ethanol, toluene, DMF or pyridine under thermal conditions with regular heating or microwave irradiation, as has been previously described by for example Lawson, Edward C.; Hoekstra, William J.; Addo, Michael F.; Andrade-Gordon, Patricia; Damiano, Bruce P.; Kauffman, Jack A.; Mitchell, John A.; Maryanoff, Bruce E.; Bioorg.Med.Chem.Lett.; (2001); *11*; 2619 – 2622.

[0284] One preferred subset of compounds of formula **Ib** are those of formula g and can be made according to the following scheme:



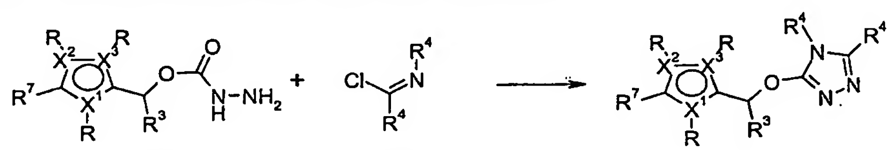
[0285] Compounds of formula **b** may be generated through selective O alkylation of a cyclic lactam **a** using Me_3OBF_4 or dimethyl sulfate (as described in literature precedences, for example: a) Sheu, Jennline; Smith, Michael B.; Oeschger, Thomas R.; Satchell, Jacqueline; Org.Prep.Proced.Int.; (1992); *24,* 147 – 158; or b) Hütchinson, Ian S.; Matlin, Stephen A.; Mete, Antonio, Tetrahedron Lett.; (2001); *42*; 1773 – 1776). The methoxy group may then be displaced by or hydrazine to form intermediate **c** which can be acylated to provide intermediate **d**. Alternatively the methoxy group may be displaced using an acyl hydrazide to yield **d** directly. Ring closing condensation to form the triazole heterocycle **e** may be done in ethanol, toluene, DMF or pyridine under thermal conditions with regular heating or microwave irradiation, as has been previously described by for example Lawson, Edward C.; Hoekstra, William J.; Addo, Michael F.; Andrade-Gordon, Patricia; Damiano, Bruce P.; Kauffman, Jack A.; Mitchell, John A.; Maryanoff, Bruce E.; Bioorg.Med.Chem.Lett.; (2001); *11*; 2619 – 2622.

[0286] A compound of formula g, wherein R^7 is selected from a group M^1-$(R^2)_n$-P-$(R^1)m_1$ may be prepared from compounds of formula **e**, by deprotonation and reaction with compounds of formula **f**. Although this can be accomplished using a strong base

due to the stabilization of the aromatic triazole ring, the reaction is facilitated when R is a group which provides additional stabilization of the resulting carbanions, such as an ester, nitrile or sulfone.

[0287] Compounds of type **XXXVII** may be prepared by the reaction of cyclic amides, lactams, which are readily alkylated in the α-position to the carbonyl by successive treatment with 2 equivalents of a strong base e.g *n*-Buli to generate the dianion followed by addition of 1 equivalent of compounds of formula **XIX**, in an aprotic solvent such as THF, as has been previously described by for example Grieco, Paul A.; Kaufman, Michael D.; J.Org.Chem.; (1999); *64*; 6041 – 6048). Alternatively, a N-protected lactam may be used in which only 1 equivalent base e.g. LDA is needed to generate the anion for the alkylation as has been previously described by for example Padwa, Albert; Beall, L. Scott; Heidelbaugh, Todd M.; Liu, Bing; Sheehan, Scott M.; J.Org.Chem.; (2000); *65*; 2684 – 2695.

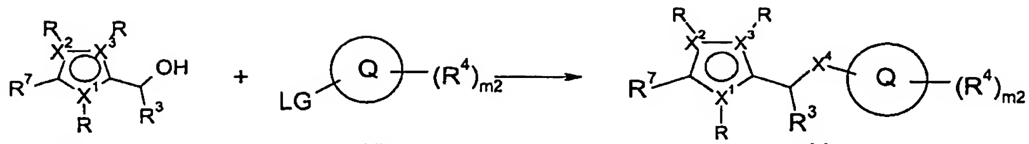
[0288] General synthesis of compounds of formula ***Ic***



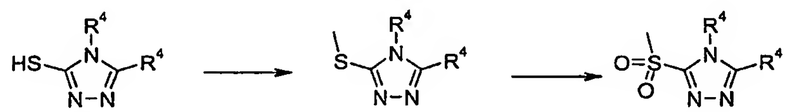
XXXVIII XXXIX Ic

[0289] A compound of formula **Ic**, wherein R^7 is consisting of M^1-$(R^2)_n$-P-$(R^1)_{m1}$, may be prepared through reaction with subsequent cyclization of compounds of formula **XXXVIII**, with a compound of formula **XXXIX**. The compound of formula **XXXIX** may be prepared from a suitable secondary amide using oxalyl chloride or pentachlorophosphine in the optional presence of a base such as triethylamine and used either in-situ or as isolated material as described above from **XXXIVa**.

[0290] Compounds of formula **XXXVIII**, may be prepared from the corresponding alcohol by reacting it with phosgene or preferably a phosgene analog such as carbonyldiimidazole followed by coupling to hydrazine.



XL XLI Id



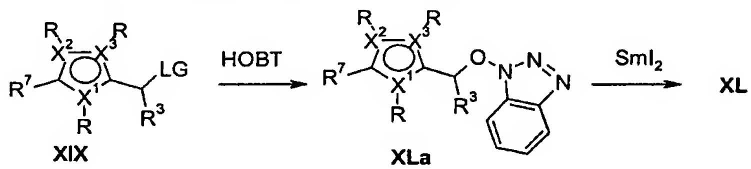
XXVI XLII XLIa

[0291] Other means of synthesizing a compound of formula **Ic** or **Id**, wherein X^4 = O and wherein R^7 is M^1-$(R^2)_n$-P-$(R^1)_{m1}$, may be by the O-alkylation of compounds of type **XL** with compounds of type **XLI** wherein the leaving group may consist of a tosyl-, mesyl-, halo- or any other appropriate group, in the a suitable base such as cesium or potassium carbonate, sodium hydride in solvents such as for example DMF or DMSO.

[0292] Compounds of type **XLI** may be synthesized as exemplified with triazole **XXVI** by alkylation or arylation of the sulfur group using an apropriate alkylating or arylating reagent followed by double oxidation of the thiogroup to the corresponding sulfone using oxidants such as MCPBA, hydrogen peroxide in acetic acid or potassium permanganate. Such a sequence has previously been described for example by Åkerblom et al. *J. Med. Chem. 16,* 312 (1973). Alternatively, triazole halides may be synthesized as previously described in the literature by for example Ashton, W.T. et al. *J. Med. Chem. 36*, 591 (1993).

[0293] The alcohols may be prepared either directly upon synthesis of the oxadiazole or isoxazole part as described above under general synthesis of compounds of formula V. Alternatively they may be prepared from an oxadiazole or isoxazole unit with an appropriate leaving group such as a halide, e.g. chloride, using a three step sequence as described by Palazzo et al. *J. Heterocycl. Chem.* (1979) 16:1469, followed by a standard reduction protocol of the resulting aldehyde (or

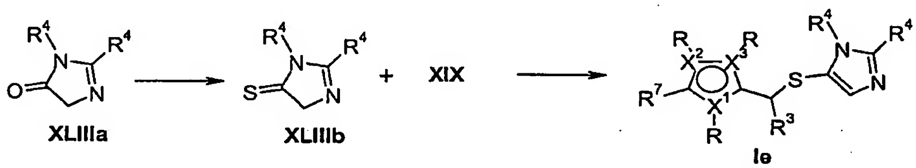
hydrate thereof) using for example sodium borohydride in methanol.



[0294] Yet another method may involve the reaction of a compound of structure XIV unit containing an appropriate leaving group such as a halide, e.g. chloride with hydroxybenzotriazole in the presence of a suitable base such as potassium carbonate or triethylamine in a suitable solvent such as DMSO, acetonitrile, acetone, DMF to give compounds of type **XLa**. Alternatively **XLa** may be obtained if hydroxybenzotriazole is present during cyclization to the oxadiazole, either as a co-activator with EDCI or as a result of a byproduct from a coupling reagent such as HBTU as described above under the reaction of compounds of formula **II - V**. **XLa** may be converted to the alcohol by the addition of samarium diiode, preferably over an elongated period of time (5-360 minutes) in a suitable solvent such as tetrahydrofuran, methanol, water or mixtures thereof, with THF being a preferred solvent, at an appropriate temperature (-75°C - +75°C).

[0295] The cleavage of the N-O bond can alternatively be done using commonly used hydrogenation methods in the presence of a suitable catalyst such as raney-nickel as known by the one skilled in the art. In compounds of formula **XLa** the oxobenzotriazole functionality may also serve as a leaving group. Thus compounds **XLa** may react with compounds **XX** as described above.

[0296] Formation of compounds of type Ie

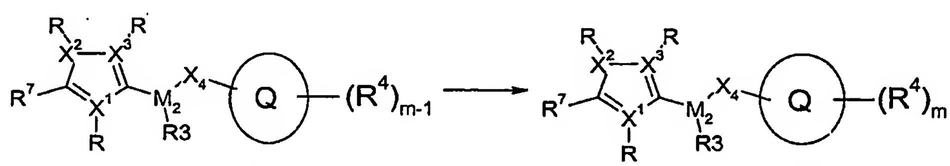


[0297] A compound of formula **Ie**, wherein R^7 is M^1-$(R^2)_n$-P-$(R^1)_{m1}$, may be prepared through nucleophilic substitution of compounds of type **XLIIIb** with compounds of type **XIX** as described above. Compounds of type **XLIIIb** may be

prepared by reaction of their oxo-analogues **XLIIIa** using P_2S_{10} or Lawesson's reagent under thermal conditions. Synthesis of compounds of type **XLIIIa** has been described by Takeuchi, H., Hagiwara, S., Eguchi, S., Tetrahedron (1989); *45*; 6375-6386.

[0298] Introduction of substitution in the Q ring:

[0299] If substitution on the Q ring is desired, one may choose an appropriately substituted aryl or heteroaryl thiol to use for the displacement reaction. The same is valid for other nucleophilic reagents other than substituted or non-substituted aryl or heteroaryl thiols serving to substitute the same in the final compounds. If the aryl or heteroaryl residue has an amenable reactive moiety, either directly introduced or as a result of a deprotection reaction, including but not limited to a free NH site as in aniline, imidazole, benzimidazole, indole and the like, a compound of formula **If** (R^7 is M^1-$(R^2)_n$-P-$(R^1)_{m1}$) may be substituted with R^4 using a suitable base such as an alkyllithium or alkali-metal hydride or hydroxide to deprotonate the NH residue, followed by the addition of a suitable electrophilic reagent such as an alkyl halides, acid chlorides or anhydrides, chloroformates, carbamoyl chlorides, sulfonyl chlorides, isocyanates, isothiocyanates and the like to provide the substituted product of Formula **Ia**.

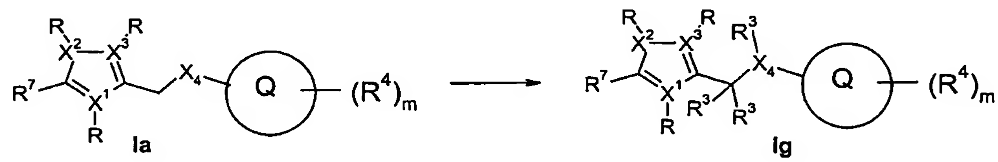


If **Ia**

[0300] Introduction of the M^2 substituent(s) and of the X^4 substituent(s):

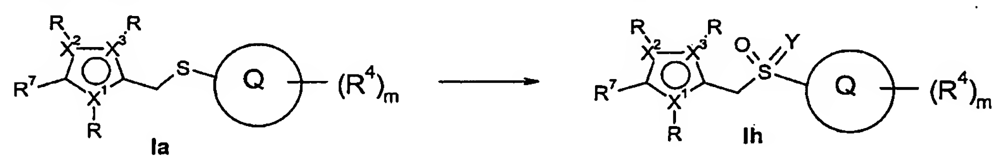
[0301] When the most acidic protons are positioned on the atom adjacent to X^4, or on X^4 itself, substitution may be achieved by deprotonation of compound of Formual **Ia** with a strong base such as an alkyllithium or an alkali-metal hydride in a suitable aprotic non-acidic solvent like THF or diethylether followed by trapping of the resulting anion with a suitable electrophile such as alkyl halides, acid chlorides or

anhydrides, chloroformates, carbamoyl chlorides, sulfonyl chlorides, isocyanates, isothiocyanates and the like. When an excess of base and electrophile are employed and the reaction is left for sufficient time, two hydrogens may be replaced by the electrophile as illustrated below for the introduction of two R^3-substituents (M^2 exemplified as carbon). Two or more, different or same substituents, might also be introduced accordingly by subsequent deprotonations and reactions with appropriate electrophiles to yield compounds of Formula **Ig**.



[0302] Oxidation of S atom of chain (when X^4 is S) or N atoms on substituents:

[0303] Oxidation of the sulfur atom to give sulfones (Y=O) and sulfoxides (Y= ":", i.e. a lone pair) may be achieved by direct oxidation using any suitable oxidizing agent including peroxyacids such as MCPBA. In the case of MCPBA oxidation, it is possible to obtain a mixture of products from a single reaction and separate them by standard column chromatography or to obtain selectively the sulfoxide or sulfone by controlling the stoichiometry and temperature of the reaction.



[0304] If one of the subsitutents, e.g. R^4 contains one or more nitrogen atoms as for example a pyridine moiety or any other susbtituent as defined above, then oxidation of this nitrogen may occur in the above reaction of **Ia** with an oxidant such as MCPBA to give the corresponding N-oxide. It is understood to the one skilled in the art that such products may be obtained by separation via standard column chromatography or any other standard purifcation protocol even in the case of mixtures containing for example **Ih** and N-oxide. It is also understood to the skilled

in the art that the formation of N-oxides may be reduced by choice of suitable reaction conditions such as using acidic media to protect the nasic amine.

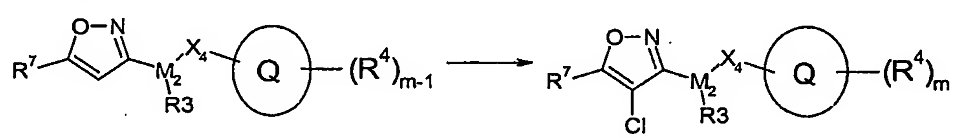
[0305] Other miscellaneous reactions:

[0306] When the intermediate compounds contain a suitable reactive functionality such as an aryl halide or triflate, the functionality may be employed to further elaborate the product. For example, when 3-halo-phenyl is present in P-$(R^1)_{m1}$, it is possible to use standard Suzuki conditions to couple an aryl boronic acid to yield a diaryl coupling product. Miyaura, N., Yanagi, T., Suzuki, A., Synth.Commun., (1981),11; 7, 513-520.

[0307] Other functionalities such as an aliphatic alcohol may for example be converted to a fluoro group by the use of a fluorinating agent such as DAST, or other halide groups by the use of for example triphenylphosphine and either iodine, N-bromosuccinimide or N-chlorosuccinimide These halides may serve as leaving groups for further elaboration or may remain as substituent in active compounds of formula **Ia**.

[0308] In a similar fashion alcohols may be transformed to leaving grous such as the non-limiting examples mesyl or tosyl by employing the appropriate sulfonyl halide or sulfonyl anhydride in the presence of a non-nucleophilic base together with the alcohol to obtain the sulfonic ester derivative.

[0309] Other functionalities which may be further elaborated are depicted in the following, non-limiting example (R^7 is M^1-$(R^2)_n$-P-$(R^1)_{m1}$), where halogenation may be undergone on a carbon-atom of an oxazole unit employing a chlorinating agent such as sulfuryl chloride.

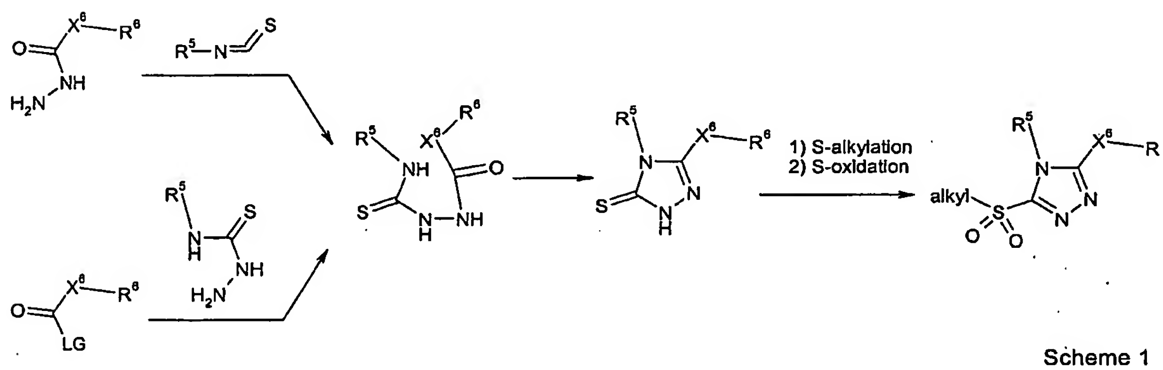


[0310] Additional Reactions for the Preparation of Intermediate and Final Compounds

[0311] More specific reaction types useful for the preparation of compounds of formula I and their intermediates, where applicable, are given below in the synthetic schemes and their corresponding descriptions. The definitions in the following formula are as defined in formula unless otherwise specified. Other starting materials are either commercially available or can be prepared via methods described in the literature.

[0312] **Intermediate Compounds**

[0313] Alkylsulphonyl[1,2,4]triazoles

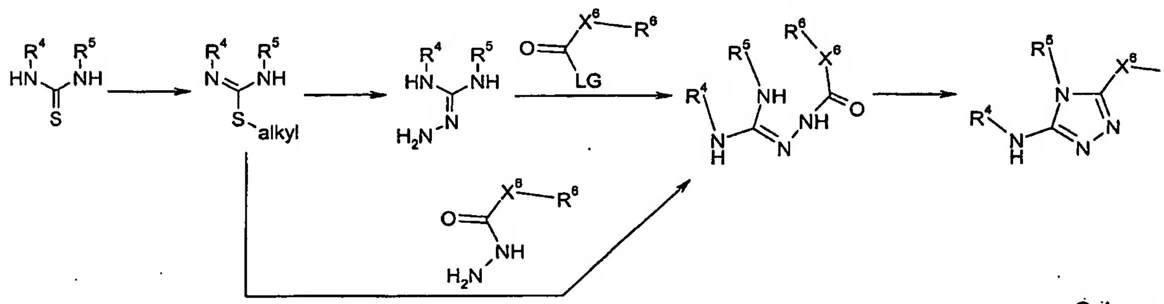


Scheme 1

[0314] With reference to scheme 1, alkylsulphonyl[1,2,4]triazoles can be prepared from the corresponding [1,2,4]triazolethiones by initial alkylation of the sulphur atom with primary alkyl halides such as MeI and EtI (alkyl is Me and Et respectively) in MeOH, EtOH, THF, acetone or the like at –30 to 100 °C, followed by oxidation of the sulphur atom using for example $KMnO_4$ in mixtures of water and acetic acid, or mCPBA in DCM, at –20 to 120 °C, or by using any other suitable oxidant. [1,2,4]triazolethiones are for example prepared by N-acylation of a thiosemicarbazide, using any suitable acylating agent such as acid chlorides (LG is Cl) in for example pyridine, or acids (LG is OH), that are activated by the treatment with standard activating reagents as described herein below, in DMF, THF, DCM or the like at –20 to 120 °C, followed by ring closure of the initially formed acyclic intermediate either spontaneously under the conditions of the acylation, or by heating

at 50 to 150 °C in pyridine or in aqueous solvents in the presence of a base, such as $NaHCO_3$ or Na_2CO_3, with or without co-solvents such as dioxane, THF, MeOH, EtOH or DMF. This acyclic intermediate can also be formed by treatment of the proper acyl hydrazide with a suitable isothiocyanate in for example 2-propanol, DCM, THF or the like at –20 to 120 °C.

[0315] Amino[1,2,4]triazoles

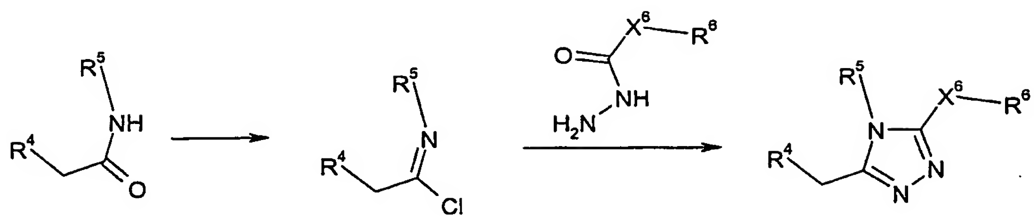


Scheme

[0316] With reference to scheme 2, amino[1,2,4]triazoles are obtained by treating carbonohydrazonic diamides with a proper acylating agent carrying a leaving group LG in suitable solvent such as THF, pyridine or DMF at -20 to 100 °C. The reaction initially leads to an open intermediate that either forms a triazole ring spontaneously, or can be made to do so by heating at 50 to 200 °C in for example pyridine or DMF. The leaving group LG may be chloro or any other suitable leaving group as for example generated by in situ treatment of the corresponding acid (LG is OH) with standard activating reagents as described herein below. Carbonohydrazonic diamides may be generated from isothioureas, in which the S-alkyl (for example S-Me or S-Et) moiety acts as a leaving group upon treatment with hydrazine in solvents such as pyridine, methanol, ethanol, 2-propanol, THF or the like at –20 to 180 °C. The open intermediate can also be directly generated by treatment of isothioureas with acylhydrazines under the same conditions as described for the reaction with hydrazine. Isothioureas are obtained by S-alkylation of the corresponding thioureas with for example MeI or EtI in acetone, EtOH, THF, DCM or the like at –100 to 100

°C.

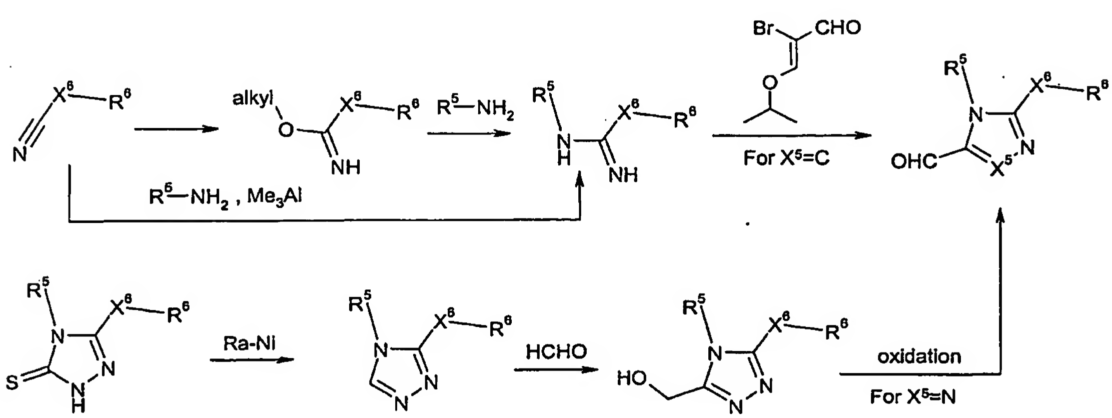
[0317] Carbon substituted [1,2,4]triazoles



Scheme 3

[0318] With reference to scheme 3, imidoyl chlorides react with acyl hydrazides in suitable solvents, such as THF, pyridine or DMF at -20 to 100 °C to initially form an open intermediate that either forms a triazole ring spontaneously, or can be made to do so by heating at 50 to 200 °C in for example pyridine, DMF or water, with or without the presence of a base such as $NaHCO_3$ or Na_2CO_3. Imidoylchlorides may in turn be obtained from the corresponding amides by standard methods such as by treatment with oxalyl chloride or thionyl chloride.

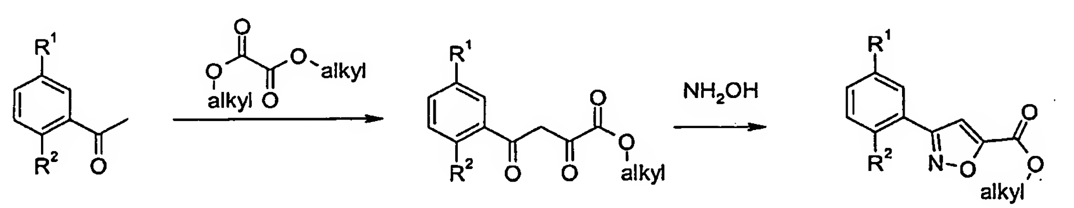
[0319] Imidazole-4-carbaldehydes and [1,2,4] triazolecarbaldehydes



Scheme 4

[0320] With reference to scheme 4, Imidazole-4-carbaldehydes (X^5 is C) are for example prepared by reacting suitably substituted amidines with 2-bromo-3-isopropoxyacrylaldehyde in for example well-stirred mixtures of an organic solvent, such as chloroform, DCM, or toluene and water in the presence of a base such as a carbonate at 10 to 100 °C. The amidine starting material might be prepared using standard methods from the corresponding nitrile via the imidate ester (alkyl is for example Me or Et), by treatment with for example a hydrochloric acid solution in the corresponding alcohol solvent followed by treatment with an amine substituted with the group R^5, or directly from the corresponding nitrile by reacting with the same amine together with trimethylaluminum. [1,2,4]triazolecarbaldehydes (X^5 is N) can be prepared by oxidizing the corresponding primary alcohols, using for example MnO_2 or any other standard oxidant for this type of transformation. These alcohols, in turn, may be prepared by hydroxymethylation of the corresponding C unsubstituted triazoles using for example formaline at elevated temperature. C unsubstituted triazoles are for example prepared through standard desulphurization of [1,2,4]triazolethiones with Raney-Ni.

[0321] Isoxazole-5-carboxylic acid esters

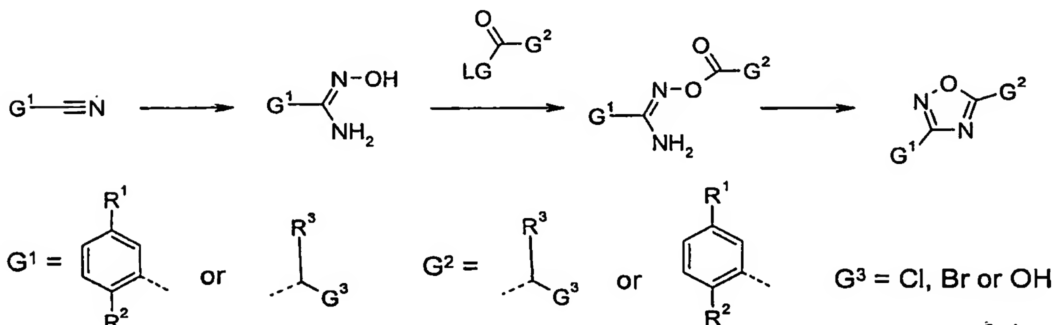


Scheme 5

[0322] In reference to scheme 5, isoxazoles are formed by reaction and *in-situ* cyclization of dioxo butyric ester derivatives with hydroxylamine hydrochloride in solvents such as ethanol, 2-propanol or DMF at temperatures from 40 to 140 °C. Dioxo butyric esters are formed through the reaction of acetophenones with dialkyl

oxolates (alkyl is for example Me or Et) in the presence of a strong base such as sodium hydride in solvents such as DMF or toluene at temperatures from –20 to 120 °C.

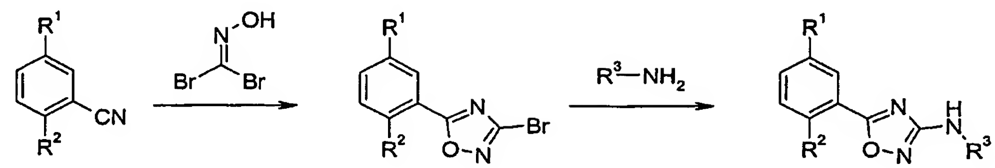
[0323] Carbon substituted [1,2,4]oxadiazoles



Scheme 6

[0324] With reference to scheme 6, [1,2,4]oxadiazoles with a carbon alpha to the heterocycle, wherein G^1, G^2 and G^3 are defined as described in scheme 6, are formed by cyclization of G^1- and G^2-substituted-acyloxyimidamides in solvents such as pyridine, DMF, or water containing mixtures thereof, at 40 to 140 °C, alternatively in aqueous alcoholic solvents in the presence of sodium acetate at temperatures from 40 to 140 °C, with the later method being preferred if one of the groups G^1 or G^2 contains a chiral stereocenter. Acyloxyimidamides are formed by coupling with a proper acylating agent carrying a leaving group LG with a G^1-substituted hydroxamidine. The leaving group LG may be chloro or any other suitable leaving group as for example generated by in situ treatment of the corresponding acid (LG is OH) with standard activating reagents as described herein below. G^1-substituted hydroxamidines are formed by reaction of the corresponding nitrile with the free base of hydroxylamine, or hydroxylamine hydrochloride in the presence of a base such as triethylamine, pyridine or sodium carbonate, in solvents such as ethanol, water or pyridine at temperatures from –20 to 120 °C

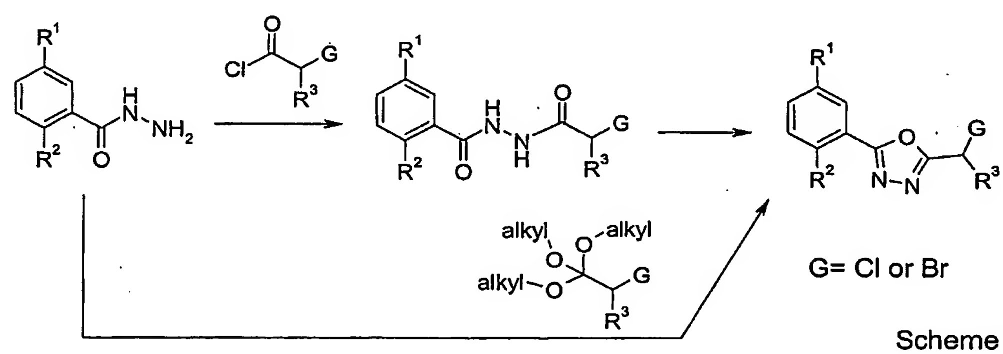
[0325] Amino[1,2,4]oxadiazoles



Scheme 7

[0326] With reference to scheme 7, amino[1,2,4]oxadiazoles are obtained from the corresponding bromo[1,2,4]oxadiazoles by reaction with an excess alkylamine in solvents such as methanol or ethanol at elevated temperatures. Intermediate bromo[1,2,4]oxadiazoles are obtained by reaction of benzonitrile derivatives with hydroxycarbonimidic dibromide in the presence of a base such as $NaHCO_3$ in solvents such as toluene or DMF at elevated temperatures.

[0327] Carbon substituted [1,3,4]oxadiazoles

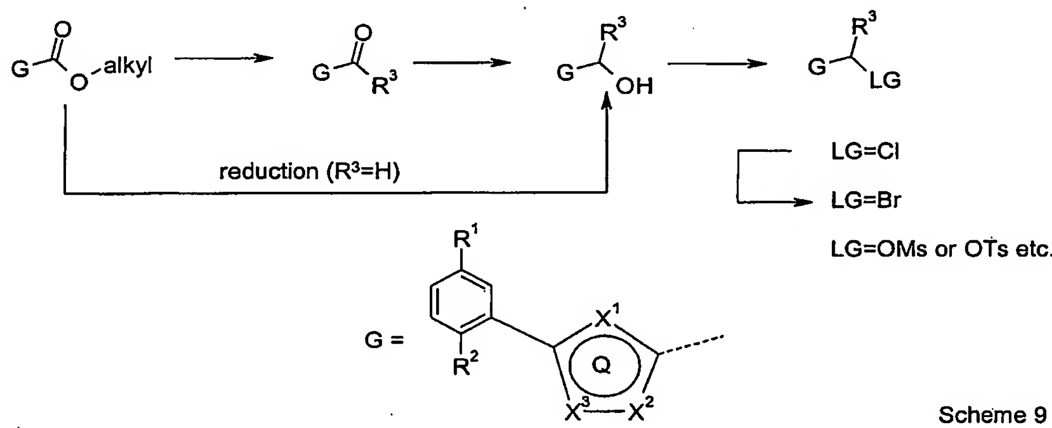


Scheme 8

[0328] With reference to scheme 8, starting from acid hydrazides, coupling with an aliphatic acid chloride derivative in THF, DMF, toluene or the like, optionally in the presence of a base such as triethylamine or a carbonate, leads to the formation of an acyl benzohydrazide derivative, which is cyclized at elevated temperatures in the

presence of a dehydrating agent such as phosphorous pentoxide in solvents such as toluene or DMF or mixtures thereof to yield the [1,3,4]oxadiazole product. Alternatively, [1,3,4]oxadiazoles may be made directly from the acid hydrazide using trialkyl ortho esters either neat or in solvents such as toluene or xylenes at elevated temperatures.

[0329] Functional group transformations

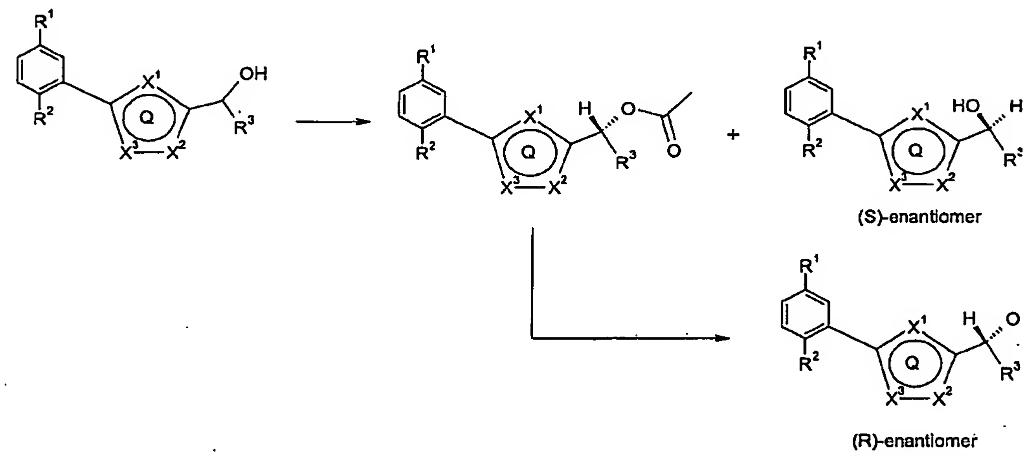


Scheme 9

[0330] With reference to scheme 9, aliphatic alcohols may for example be converted by standard methods to the corresponding halides by the use of for example triphenylphosphine in combination with either iodine, N-bromosuccinimide or N-chlorosuccinimide, or alternatively by treatment with tribromo phosphine or thionylchloride. In a similar fashion alcohols may be transformed to other leaving groups such as mesylates or tosylates by employing the appropriate sulfonyl halide or sulfonyl anhydride in the presence of a non-nucleophilic base together with the alcohol to obtain the corresponding sulfonates. Clorides or sulphonates can be converted to the corresponding bromides or iodides by treatment with bromide salts, for example LiBr, or iodide salts. Further standard methods to obtain alcohols include the reduction of the corresponding carbonyl containing groups such as methyl or ethyl esters, aldehydes (R^3 is H) or ketones (R^3 is not H), by employing common

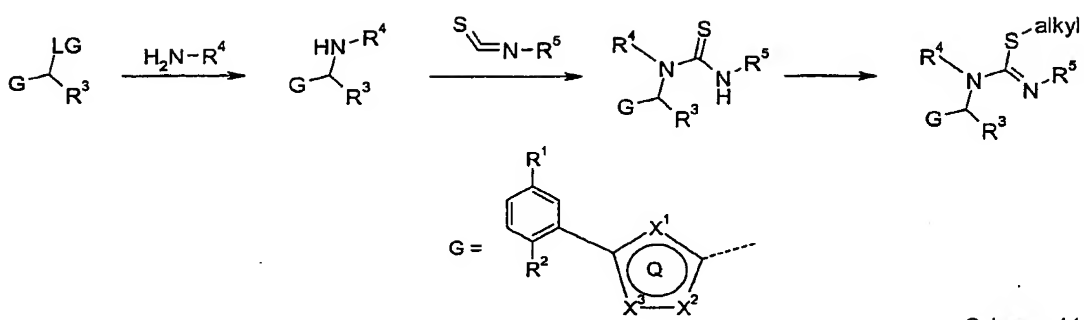
reducing agents such as boranes, lithium borohydride, lithium aluminiumhydride, or hydrogen in the presence of a transition metal catalyst such as complexes of for example ruthenium or iridium, or alternatively palladium on charcoal.

[0331] Stereoselective preparation of chiral secondary alcohols



Scheme

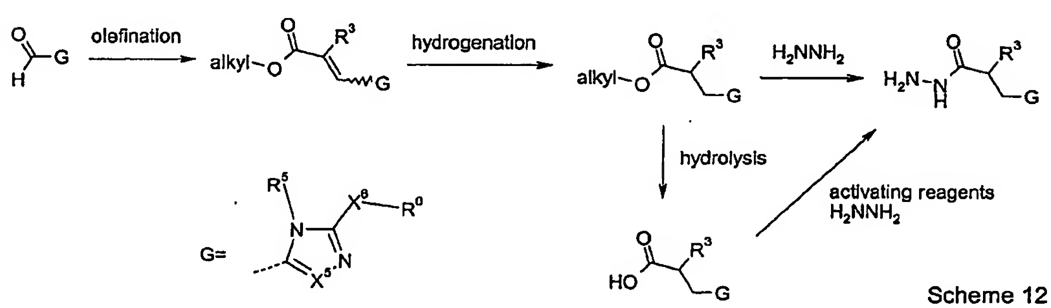
[0332] Enantiomerically pure or enriched products as depicted in scheme 10 (R^3 is Me or Et) are obtained by kinetic resolution of racemic or scalemic secondary alcohols using enzyme-catalyzed acetylation with for example polymer bound *Candida Antarctica Lipase* (Novozyme 435®), or other esterases, for example *Candida rugosa* or *Pseudomonas fluorescens*, in organic solvents such as toluene, tert-butyl methyl ether, tert-butanol or DCM at temperatures from 0 to 90 °C, using acetylating reagents such as vinyl acetate, other substitued alkyl acetates, pentafluorophenyl acetate or nitro- or halophenyl acetates, which yields the enriched (*R*)-acetate and the enriched (*S*)-alcohol. The (*R*)-acetate may be hydrolyzed to the corresponding alcohol by e.g. lithium hydroxide in mixtures of THF and water or by any other methods as described herein below, to yield the opposite enantiomerically enriched or pure alcohol.



Scheme 11

[0334] Isothioureas, as depicted in scheme 11, may be obtained by substitution of a leaving group LG (LG is for example Cl, Br or OMs) by a R^4-substituted amine in solvents such as MeOH or EtOH at temperatures from 0 to 150 °C. The product is added to an isocyanate substituted with R^5 in solvents such as chloroform, ethanol, methanol or DMF at temperatures from -20 to 100 °C, yielding a thiourea intermediate, which may be alkylated by an alkylating agent such as methyl- or ethyliodide or any other suitable primary alkyl halide or sulphonate, in solvents such as methanol, ethanol, acetonitrile or acetone, in the presence or absence of a base such as triethylamine or potassium carbonate.

[0335] Propionic acid derivatives



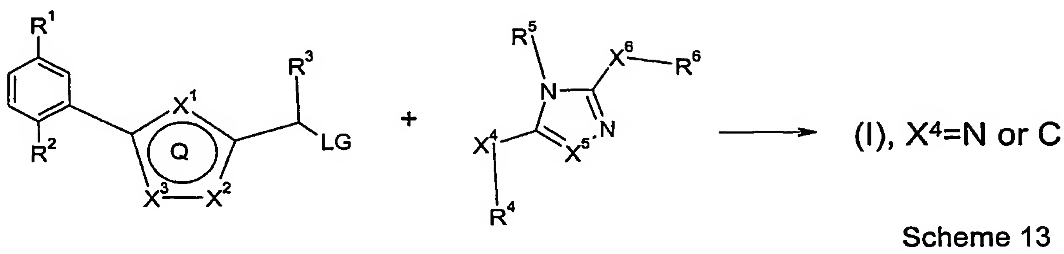
Scheme 12

[0336] Propionic acid derivatives such as saturated alkyl esters, saturated free carboxylic acids or saturated acyl hydrazides may be prepared as depicted in scheme 12. Carboxylic acids are obtained upon hydrolysis of the corresponding esters for example under basic conditions such as sodium hydroxide in methanol or any other method known to the one skilled in the art. The corresponding saturated alkyl esters in turn may be obtained from the unsaturated ester by reduction of the carbon-carbon double bond using hydrogen at atmorpheric pressure or elevated pressures up to 100 bars in the presence of a metal catalyst such as palladium on charcoal or any other selective reducing agent suitable for this type of compounds as known to the one skilled in the art. During aforementioned hydrogenation, any halide substituents attached to aromatic groups R^6 will be removed by hydro-dehalogenation. Unsaturated esters in turn may be obtained by an olefination reaction such as the Wittig or Horner-Wadsworth-Emmons type by reacting an aldehyde or ketone in the presence of a suitable base such as n-BuLi or DBU with appropriately substitued phosphor ylides or phosphonates such as triethyl-2-phosphonopropionate, or 2-(diethoxy-phosphoryl)-propionic acid ethyl ester in suitable solvents such as acetonititrile or THF at temperatures from -90 to 100 °C. Acyl hydrazides may be obtained from the corresponding esters by reaction with hydrazine, or from the free carboxylic acids by activation as described herein below and coupling with hydrazine.

[0337] Preparation of final compounds

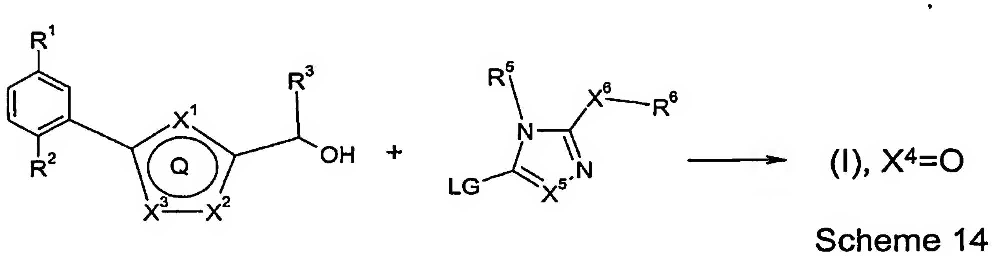
[0338] Several non-limiting methods for preparing the final compounds are illustrated and exemplified by drawings in which the generic groups, or other structural elements of the intermediates correspond to those of formula I. It is to be understood that an intermediate containing any other generic group or structural element than those of formula I can be used in the exemplified reactions, provided that this group or element does not hinder the reaction and that it can be chemically converted to the corresponding group or element of formula I at a later stage which is known to the one skilled in the art.

[0339] By connection to nucleophilic X^4



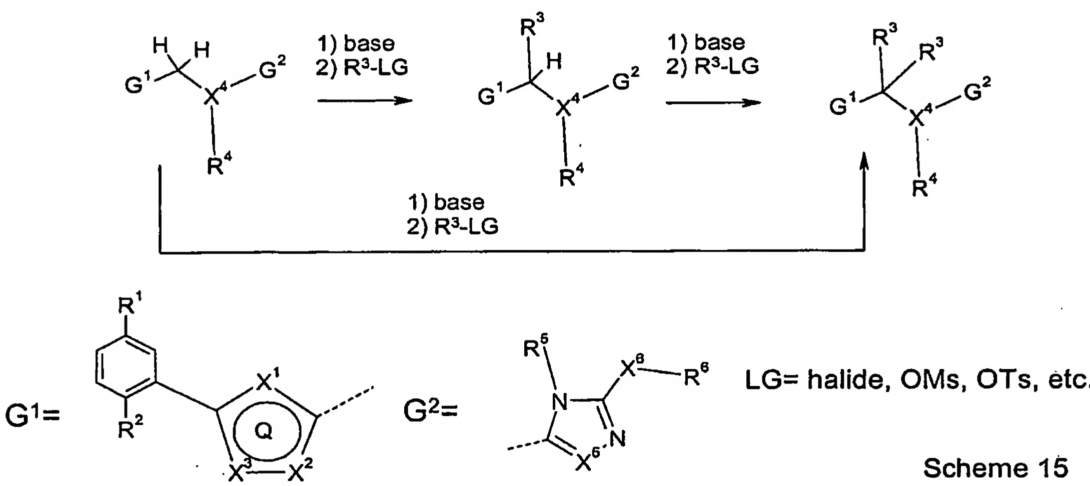
[0340] With reference to scheme 13, compounds of formula I can be prepared by bond formation through nucleophilic replacement of a leaving group (LG) in which X^4 is acting as nucleophile. X^4 can be a carbon or nitrogen atom in it's anionic form, generated by treatment of the corresponding protonated neutral atom with bases in suitable solvents such as LDA or nBuLi in THF, diethylether or toluene, or NaH in for example DMF, or K_2CO_3 in acetonitile or ketones such as 2-butanone at a temperature from –100 to 150 °C. When X^4 is carbon, LG is preferable bromo, and when X^4 is nitrogen examples of suitable leaving groups LG are chloro, bromo, OMs and OTs. When X^4 is N, the reaction may also be undertaken in a stereoselective manner by employing enantiomerically pure or enriched starting materials in which the leaving group LG is attached to the stereocenter. Optionally, catalytic or stochiometric amounts of an alkali metal iodide, such as LiI, can be present in the reaction to facilitate the same through *in situ* displacement of the leaving group to iodo.

[0341] By connection to nucleophilic oxygen



[0342] With reference to scheme 14, compounds of formula I can be prepared by bond formation through nucleophilic replacement of a leaving group (LG) in which an alcohol is acting as O-nucleophile under basic conditions to facilitate the reaction. As base, for example NaH or Cs_2CO_3 is used, the latter being preferred for obtaining enantiomerically pure products, at temperatures from 0 to 100 °C in polar aprotic solvents such as DMF or acetonitrile. Examples of suitable leaving groups are sulphonates such as OMs and halogens such as chloro.

[0343] By alpha-alkylation relative to ring Q

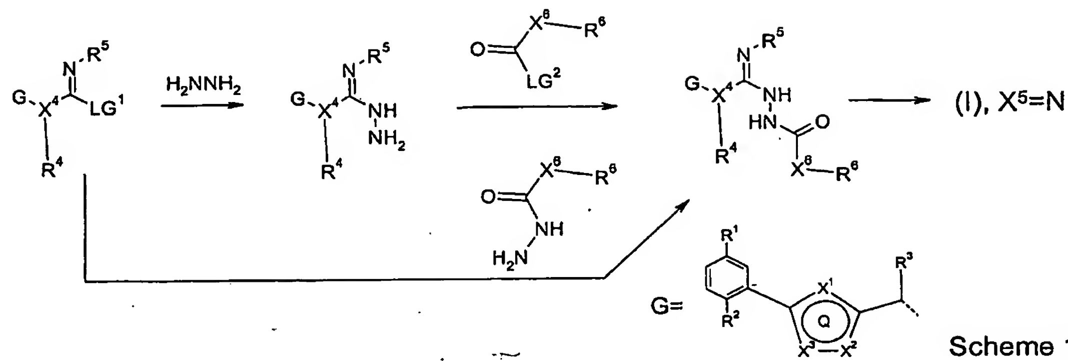


Scheme 15

[0344] With reference to scheme 15, compounds of formula I substituted with no group R^3 can be either mono- or dialkylated at the position *alpha* to ring Q. Dialkylation can be performed sequentially for the introduction of two different or same groups R^3. Preferably, primary alkyl halides, mesylates, or tosylates are used as alkylating reagents (R^3-LG) in the reaction with an intermediate carbanionic nucleophile generated upon treatment of compounds of formula I, substituted with no or one group R^3, with strong bases such as NaH, LDA or HMDS alkali metal salts in solvents such as for example THF, diethylether, hexanes or toluene at a temperature

of –100 to 50 °C.

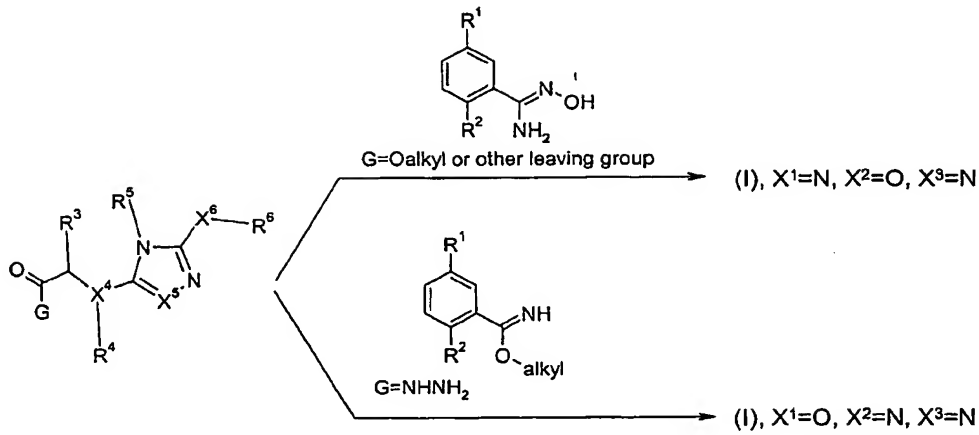
[0345] By formation of a triazole ring



Scheme 16

[0346] With reference to scheme 16, intermediates carrying a leaving group LG^1, such as SMe or SEt, can undergo reaction with hydrazine in solvents such as pyridine, methanol, ethanol, 2-propanol, THF or the like at –20 to 180 °C. Subsequent acylation with an acylating agent carrying a leaving group LG^2 in suitable solvent such as THF, pyridine or DMF at 0 to 100 °C leads to an open intermediate that either forms a triazole ring spontaneously, or can be whipped to do so by heating at 50 to 200 °C, resulting in the formation of a compound of formula I. LG^2 may be chloro or any other suitable leaving group as for example generated by *in situ* treatment of the corresponding acid (LG^2=OH) with standard activating reagents such as DCC, DIC, EDCl or HBTU, with or without the presence of co-reagents such as HOBt or DMAP in suitable solvents such as DMF, DCM, THF, or acetonitrile at a temperature from –20 to 100 °C. Alternatively, acylhydrazines can be directly reacted with intermediates carrying a leaving group LG^1 under the conditions described above to yield compounds of formula I.

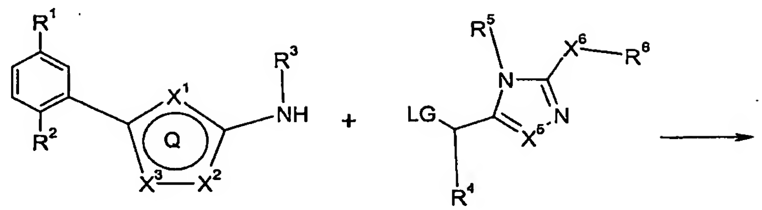
[0347] By formation of the ring Q



Scheme 17

[0348] With reference to scheme 17, the ring Q of compounds of formula I may be formed by reaction of esters (G is for example OMe or OEt) or activated acid derivatives, such as acid chlorides (G is Cl) or else as generated upon treatment of the corresponding acids (G is OH) with standard activating reagents as described herein above, with N-hydroxyamidines. When employing esters, suitable conditions include the use of the solvents 1-propanol, 2-propanol, EtOH or toluene, together with a stochiometric amount of a base such as potassium tert-butoxide at 0 to 180 °C. When employing activated acid derivatives the reaction can for example be run in DMF, DCM, THF, pyridine or the like at –20 to 120 °C. The initially formed acyclic intermediate may ringclose spontaneously to form an [1,2,4]oxadiazole, or may be heated in pyridine, DMF, EtOH, MeOH or aqueous mixtures thereof, with or without additives such as sodium acetate, at 50 to 200 °C. Upon reaction of acyl hydrazides (G is $NHNH_2$) with imidate esters (alkyl is for example Me or Et), or the corresponding salts, in MeOH, EtOH, THF, DMF or the like at 0 to 150 °C, compounds of formula I in which the ring Q is [1,3,4]oxadiazole are generated.

[0349] By N-alkylation of heterocyclic amines



(I), X^4=C, X^7=C

Scheme 18

[0350] With reference to scheme 18, compounds of formula I are prepared by bond formation through nucleophilic replacement of a leaving group (LG) in which the nitrogen atom, to which the group R^3 is attached, is acting as nucleophile. The reaction is facilitated by deprotonation of this nitrogen atom to generate a stronger nucleophile by treatment with bases in suitable solvents such as LDA, alkali metal salts of HMDS or nBuLi in THF, diethylether or toluene, or NaH in for example DMF at a temperature from –100 to 150 °C. Suitable leaving groups include for example chloro, bromo, iodo, OMs or OTs. Useful intermediates carrying such a leaving group can for example be prepared by halogenation of the corresponding compound in which LG is hydrogen. For example, *alpha*-chloro triazoles (LG is Cl and X^5 is N) can be prepared by treatment with SO_2Cl_2 in solvents such as DCM and DMF.

[0351] By cytochrome P450 mediated dealkylation

[0352] Compounds of formula I in which X^4 is nitrogen and R^4 is alkyl, preferably methyl, can be converted to the corresponding compounds in which R^4 is hydrogen by incubation with human liver microsome protein, or other sources of cytochrome P450 isoenzymes including preferably the 3A4 isoenzyme, at 35-40 °C in for example aqueous phosphate buffer in the presence of NADPH.

[0353] By chromatographic separation of enantiomers

[0354] Practically pure (>95%) enantiomers of compounds of formula I can be obtained by chromatographic separation of the corresponding racemic or scalemic

mixtures by using for example Chiralpak AD® or Chiracel OJ® as stationary phase and for example 2-propanol or ethanol, and mixtures of hexanes and ethanol respectively, as eluants.

[0355] Examples

[0356] Suitable embodiments of the invention will now be illustrated by the following non-limiting examples.

[0357] NMR measurements were made on the delta scale (δ).

[0358] The compounds prepared according to Examples 1 to 39 and 100 to 328 are intermediates.

[0359] The compounds prepared according to Examples 40 to 99 and 329 to 794 are end products.

[0360] Intermediates

[0361] Example 1

[0362] 6-Methylpyridine-4-carboxylic acid

[0363] A hydrogen filled balloon was attached to a flask containing 2-chloro-6-methylpyridine-4-carboxylic acid (2 g, 12.0 mmol), palladium 10 wt. % on activated carbon (0.5 g), triethyl amine (4.8 ml) and ethanol (24 ml) and then stirred overnight at room temperature. The reaction mixture was filtered through celite, washed with methanol and concentrated. The residue was titurated with dichloromethane and then filtered to afford 6-methylpyridine-4-carboxylic acid as a white solid; 1.05 g (66%). ^{1}H NMR (MeOD) δ (ppm): 8.62 (d, 1H), 7.68 (s, 1H), 7.60 (d, 1H), 2.55 (s, 3H).

[0364] Example 2

[0365] 1-Cyano-3-ethylbenzene

[0366] Argon was bubbled into a solution of 1-bromo-3-ethylbenzene (2.5 g, 13.5 mmol) in DMF (37 ml) for 10 min. and then zinc cyanide (1.75 g, 14.9 mmol) and tetrakis(triphenylphosphine)palladium(0) (1.56 g, 1.35 mmol) were added. After

stirring at 80°C overnight the reaction mixture was diluted with ethyl acetate (35 ml) then filtered through celite to remove the precipitate. The filtrate was washed with water (3x), saturated brine, dried over anhydrous sodium sulfate, filtered and concentrated. The product was purified by flash column chromatography using 2% ethyl acetate in hexane affording a colorless liquid (1.42 g). GC-MS (M+): 131.18.

[0367] Example 3

[0368] 3-Ethylbenzoic acid

[0369] 6 M Sodium hydroxide (25 ml) was added to 1-cyano-3-ethylbenzene (1 g, 7.62 mmol) in methanol (25 ml) and then heated at 100°C overnight. After concentrating the reaction mixture, the aqueous layer was washed with dichloromethane (2x), then acidified pH about 3 with 12 M HCl. The precipitate was extracted with ethyl acetate then washed with water and saturated brine, dried over anhydrous sodium sulfate, filtered and concentrated to afford 3-ethylbenzoic acid as a colorless oil; 0.770 g (28% yield over 2 steps). ^{1}H NMR ($CDCl_3$), δ (ppm): 7.76 (d, 2H), 7.43 (m, 2H), 2.67 (m, 2H), 1.19 (t, 3H).

[0370] Example 4

[0371] 3-Fluoro-5-methyl-benzoic acid

[0372] Concentrated HCl (30 ml) was added to a cooled (-5°C) suspension of dimethyl 5-amino isophthalate (20 g, 95.6 mmol) in water (75 ml), followed by portionwise addition of $NaNO_2$ (7.5 g, 109 mmol). The reaction mixture was then stirred for 15 min., after which HBF_4 (18 ml, 100 mmol, 48% aqueous solution) was added. The resulting mixture was stirred at 0°C for 30 min. and the precipitate formed was collected by filtration and washed with cold methanol (60 ml) and ether (60 ml). The residue was then decomposed by heating in an oil bath (~110°C). The cooled mixture was then diluted with ether, concentrated onto silica gel and purified by flash chromatography with 5% ethyl acetate hexane as eluant giving 9.0 g (44%) of product as a white fluffy solid. ^{1}H NMR ($CDCl_3$), δ (ppm): 8.57 (s, 1H), 7.95 (d, 2H), 3.97 (s, 6H).

[0373] A suspension of 5-fluoro-isophthalic acid dimethyl ester (1.7 g, 8.0 mmol) in

methanol (41 ml) was treated with 1.0 N sodium hydroxide (7.2 ml, 7.2 mmol). The reaction was left stirring overnight at room temperature. After the solution was concentrated, the residue was dissolved in water and transferred to a separatory funnel. The aqueous layer was washed with dichloromethane (3 times) and then acidified with 1.0 N HCl to pH 2. Ethyl acetate was used to extract the precipitate, which was then washed with brine and dried over anhydrous sodium sulphate. After removal of solvent in vacuo, a total of 1.3 g (83%) of 5-fluoro-isophthalic acid monomethyl ester was isolated as a white solid. ^1H NMR (DMSO), δ (ppm): 8.31 (t, 1H), 7.96 (m, 2H), 3.91 (s, 3H).

[0374] Triethylamine (2.2 ml, 16.0 mmol) and isobutyl chloroformate (1.0 ml, 8.0 mmol) were added to an ice-cooled solution of 5-fluoro-isophthalic acid monomethyl ester (1.3 g, 6.7 mmol) in dichloromethane (20 ml) and then warmed to room temperature. After stirring for 2 h, the reaction mixture was filtered and concentrated. The residue was re-dissolved tetrahydrofuran (10 ml) and then sodium borohydride (1.1 g, 29.02 mmol) in water (3ml) was added drop-wise. After 1 h, the reaction was quenched with methanol and then diluted with ethyl acetate, washed with water and brine, dried over anhydrous sodium sulfate, filtered and concentrated. Flash column chromatography on silica gel using 30% ethyl acetate in hexanes afforded 667 mg (54%) of 3-fluoro-5-hydroxymethyl-benzoic acid methyl ester as a colorless oil. ^1H NMR ($CDCl_3$), δ (ppm): 7.82 (s, 1H), 7.63 (d, 1H), 7.32 (d, 1H), 4.76 (s, 2H), 3.93 (s, 3H).

[0375] Ethanol (2 ml) was added to round bottom flask containing 3-fluoro-5-hydroxymethyl-benzoic acid methyl ester (667 mg, 3.6 mmol) and palladium (10 wt.% on activated carbon, 300 mg) under argon. The flask was evacuated using a water aspirator and then filled with hydrogen from a balloon. After stirring for 2 h, the palladium on carbon was removed by filtration through celite. The filtrate was then concentrated to afford 520 mg (87%) of 3-fluoro-5-methyl-benzoic acid methyl ester. ^1H NMR ($CDCl_3$), δ (ppm): 7.65 (s, 1H), 7.51 (d, 1H), 7.08 (d, 1H), 3.91 (s, 3H), 2.40 (s, 3H).

[0376] 0.5 N Lithium hydroxide (7.4 ml, 3.7 mmol) was added to a solution 3-fluoro-5-methyl-benzoic acid methyl ester (520 mg, 3.1 mmol) in tetrahydrofuran (7.4

ml). The reaction was stirred at 75°C for 2 h and then the solvent was removed in vacuo. The residue was dissolved in a small amount of water and then acidified (pH about 2) by the addition of 10% HCl (aq.). Following extraction of the aqueous layer with ethyl acetate, the organic layer was then washed with water and saturated brine, dried over anhydrous sodium sulfate, filtered, and concentrated to afford 469 mg (98%) of 3-fluoro-5-methyl-benzoic acid as a white solid. 1H NMR (DMSO), d (ppm): 7.62 (s, 1H), 7.45 (d, 1H), 7.32 (d, 1H), 2.38 (s, 3H).

[0377] Example 5

[0378] 3-Methoxymethyl-benzoic acid

[0379] A mixture of 3-bromomethyl-benzoic acid methyl ester (556 mg, 2.4 mmol) and potassium carbonate (670 mg, 4.9 mmol) in methanol (10 ml) and tetrathydrofuran (10 ml) was heated at 55°C for 2 h. After cooling, the reaction mixture was diluted with water and then extracted with ethyl acetate. The organic layer was washed with water and saturated brine, dried over anhydrous sodium sulfate, filtered and concentrated. After drying in vacuo, 3-methoxymethyl-benzoic acid methyl ester (436 mg, quantitative) was isolated as a white solid. ^{1}H NMR ($CDCl_3$), δ (ppm): 8.01 (s, 1H), 7.98 (d, 1H), 7.55 (d, 1H), 7.43 (t, 1H), 4.50 (s, 2H), 3.92 (s, 3H), 3.41 (s, 3H).

1 N Sodium hydroxide (3.6 ml, 3.6 mmol) was added to a 3-methoxymethyl-benzoic acid methyl ester (436 mg, 2.4 mmol) in methanol (5 ml) and tetrahydrofuran (5 ml). The reaction was stirred at 70°C for 30 min. and then the solvent was removed in vacuo. The residue was dissolved in a small amount of water and then acidified (pH about 2) by the addition of 1 N HCl (aq.). Following extraction of the aqueous layer with ethyl acetate, the organic layer was then washed with water and saturated brine, dried over anhydrous sodium sulfate, filtered, and concentrated to afford 395 mg (98%) of 3-methoxymethyl-benzoic acid as a white solid. ^{1}H NMR (DMSO), δ (ppm): 7.90 (s, 1H), 7.87 (d, 1H), 7.56 (d, 1H), 7.48 (t, 1H), 4.48 (s, 2H), 3.31 (s, 3H).

[0380] Example 6

[0381] ***N*****-Hydroxy-3-methoxy-benzamidine**

[0382] Using the general procedure of Shine et al., J. Heterocyclic Chem. (1989) 26:125-128, hydroxylamine hydrochloride (22 ml, 5 M, 110 mmol) and sodium hydroxide (11 ml, 10 M, 110 mmol) were added to a solution of 3-methoxybenzonitrile (11.5 ml. 94 mmol) in ethanol (130 ml). The reaction mixture was then heated at reflux (80°C) for 12 h. After the mixture was cooled, most of the solvent was removed in vacuo. The crude product was partitioned between ethyl acetate and water, washed with saturated brine, dried over anhydrous sodium sulfate and the solvent was removed in vacuo. Flash chromatography on silica gel using 35-50% ethyl acetate in hexane yielded the title compound (8.05 g, 52%).

Examples 7-9 were prepared in an analogous method to the procedure given in Example 6.

[0383] **Example 7**

[0384] ***N*-Hydroxy-benzamidine**

[0385] *N*-hydroxy-benzamidine (4.83 g, 91%, white solid) was obtained from benzonitrile (4 g, 38.9 mmol), hydroxylamine hydrochloride (8.89 ml, 44.0 mmol) and sodium hydroxide (4.49 ml, 45.0 mmol) in ethanol (30 ml). ^{1}H NMR ($CDCl_3$), δ (ppm): 8.81 (broad peak, 1H), 7.63 (m, 2H), 7.39 (m, 3H), 4.91 (s, 2H).

[0386] **Example 8**

[0387] ***N*-Hydroxy-3-methyl-benzamidine**

[0388] *N*-Hydroxy-3-methyl-benzamidine (3.65 g, 94%, white solid) was obtained from m-tolunitrile (3 g, 26.0 mmol), hydroxylamine hydrochloride (5.9 ml, 29.6 mmol), and sodium hydroxide (3.0 ml, 29.9 mmol) in ethanol (20 ml). ^{1}H NMR ($CDCl_3$), δ (ppm): 8.25 (broad peak, 1H), 7.36 (m, 2H), 7.25 (m, 2H), 4.88 (s, 2H), 2.38 (s, 3H).

[0389] **Example 9**

[0390] **3-Cyano-*N*-hydroxy-benzamidine**

[0391] 3-Cyano-*N*-hydroxy-benzamidine (1.32 g, 52%, white solid) was obtained from isophthalonitrile (2 g, 15.6 mmol), hydroxylamine hydrochloride (3.12 ml, 5 M,

15.6 mmol) and sodium hydroxide (15.6 ml, 1 M, 15.6 mmol) in ethanol (20 ml). Purification was performed by flash column chromatography using 20-50% ethyl acetate in hexanes. ^{1}H NMR (DMSO), δ (ppm): 9.91 (s, 1H), 8.06 (s, 1H), 8.01 (d, 1H), 7.85 (d, 1H), 7.59 (t, 1H), 6.01 (bs, 2H).

[0392] Example 10

[0393] **5-Chloromethyl-3-(3-methoxy-phenyl)-[1,2,4]oxadiazole**

[0394] Chloroacetyl chloride (0.72 ml, 9.03 mmol) and triethylamine (1.50 ml, 10.23 mmol) were added to *N*-hydroxy-3-methoxy-benzamidine (1 g, 6.02 mmol) in dichloromethane (12.0 ml) at 0$^{\circ C}$ and the resulting mixture was stirred for 20 min. To effect cyclization to oxadiazole, the solution was concentrated and DMF (20 ml) was added to the residue and heated at 120$^{\circ C}$ for 5 h. The product was purified by flash chromatography using 10-20% ethyl acetate in hexane affording 0.90 g (66% yield over 2 steps) of the title compound (yellow oil). ^{1}H NMR ($CDCl_3$), δ (ppm): 7.68 (m, 1H), 7.60 (d, 1H), 7.40 (t, 1H), 7.07 (m, 1H), 4.76 (s, 2H), 3.88 (s, 3H).

[0395] Examples 11-14 were prepared in an analogous method to the procedure given in Example 10.

[0396] Example 11

[0397] **5-Chloromethyl-3-phenyl-[1,2,4]oxadiazole**

[0398] 5-Chloromethyl-3-phenyl-[1,2,4]oxadiazole (1.62 g, 57% yield over 2 steps, yellow oil) was obtained from chloroacetyl chloride (1.76 ml, 22.05 mmol) and triethylamine (3.32 ml, 24.99 mmol) with *N*-hydroxy-benzamidine (2 g, 14.7mmol) in dichloromethane (29.3 ml). Purification was performed by flash chromatography using 10% ethyl acetate in hexane. ^{1}H NMR ($CDCl_3$), δ (ppm): 8.08 (m, 2H), 7.51 (m, 3H), 4.76 (s, 2H).

[0399] Example 12

[0400] **5-Chloromethyl-3-m-tolyl-[1,2,4]oxadiazole**

[0401] 5-Chloromethyl-3-m-tolyl-[1,2,4]oxadiazole (1.75 g, 62% yield over 2 steps,

yellow oil) was obtained from chloroacetyl chloride (1.59 ml, 20.0 mmol) and triethylamine (3.00 ml, 22.7 mmol) with *N*-hydroxy-3-methyl-benzamidine (2 g, 13.3 mmol) in dichloromethane (26.6 ml). Purification was performed by flash chromatography using 10% ethyl acetate in hexane. ^{1}H NMR ($CDCl_3$), δ (ppm): 7.90 (s, 1H), 7.87 (s, 1H), 7.36 (m, 2H), 4.75 (s, 2H), 2.34 (s, 3H)

[0402] Example 13

[0403] 3-(3-Chloromethyl-[1,2,4]oxadiazol-5-yl)-benzonitrile

[0404] 3-(3-Chloromethyl-[1,2,4]oxadiazol-5-yl)-benzonitrile (3.57 g, 43%) was obtained from 2-chloro-*N*-hydroxy-acetamidine (4.05 g, 37.4 mmol) and 3-cyanobenzoyl-chloride (6.2 g, 37.4 mmol) in dichloromethane (60 ml) with triethylamine (6.5 ml, 46.7 mmol).. Purification was performed by silica gel chromatography. ^{1}H NMR ($CDCl_3$), δ (ppm): 8.47 (bs, 1H), 8.41 (dd, 1H), 7.91 (dd, 1H), 7.72(t, 1H), 4.70 (s, 2H); GC-MS (M+): 219.

[0405] Example 14

[0406] 3-(5-Chloromethyl-[1,2,4]oxadiazol-3-yl)-benzonitrile

[0407] 3-(5-Chloromethyl-[1,2,4]oxadiazol-3-yl)-benzonitrile (1.2 g, 87%, light brown solid): 3-cyano-*N*-hydroxy-benzamidine (1.0 g, 6.2 mmol), triethylamine (1.5 ml, 10.6 mmol) and chloroacetyl chloride (0.74 ml, 9.3 mmol) in dichloromethane (12 ml). Purification was performed by decolorizing with silica gel. 1H NMR (CDCl3), d (ppm): 8.40 (s, 1H), 8.32 (d, 1H), 7.82 (d, 1H), 7.64 (t, 1H), 4.77 (s, 2H).

[0408] Example 15

[0409] 3-Chloromethyl-5-m-tolyl-[1,2,4]oxadiazole

[0410] 3-Methyl-benzoyl chloride (0.80 ml, 6.1 mmol) was added to a solution of 2-chloro-*N*-hydroxy-acetamidine (440 mg, 4.1 mmol) in dichloromethane (10 ml) at room temperature and the resulting mixture was stirred for 30 min. Then triethylamine (0.62 ml, 4.5 mmol) was added and the resulting mixture was stirred for 30 min. The product was partitioned into dichloromethane and the organic layer was washed with water and brine and dried over sodium sulfate. Evaporation of the

solvent and flash chromatography on silica (10 – 20% ethyl acetate in hexanes) yielded the acyclic ester intermediate (814 mg). A solution of this intermediate in DMF (10 ml) was heated at 135°C for 4 h. The product was partitioned into ethyl acetate and the organic layer was washed with water and brine and dried over sodium sulfate. Evaporation of the solvent and flash chromatography on silica (5% ethyl acetate in hexanes) yielded 3-chloromethyl-5-m-tolyl-[1,2,4]oxadiazole (469 mg, 54% over 2 steps, white solid). ^{1}H NMR ($CDCl_3$), δ (ppm): 7.99 (s, 1H), 7.97 (m, 1H), 7.43 (d, 2H), 4.68 (s, 2H), 2.45 (s, 3H).

[0411] Example 16

[0412] 3-Chloromethyl-5-(3-fluoro-phenyl)-[1,2,4]oxadiazole

[0413] DMF (10 ml) was added to a mixture of 3-fluorobenzoic acid (710 mg, 5.07 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDCI) (972 mg, 5.07 mmol), 1-hydroxybenzotriazole hydrate (HOBt) (685 mg, 5.07 mmol) and 2-chloro-*N*-hydroxy-acetamidine (500 mg, 4.61 mmol) at room temperature and then stirred overnight. The reaction mixture was diluted with ethyl acetate, washed with water (3 times) and brine, dried over anhydrous sodium sulfate, filtered and concentrated. DMF (14 ml) was added to the residue and the resulting solution was heated at 135$^{\circ C}$ for 3.5 h to effect cyclization to oxadiazole. After cooling the reaction mixture was washed with water (3 times) and brine, dried over anhydrous sodium sulfate, filtered and concentrated. 3-Chloromethyl-5-(3-fluoro-phenyl)-[1,2,4]oxadiazole (383 mg, 35% yield over 2 steps, yellow oil) was obtained by flash chromatography on silica gel, using 5% ethyl acetate in hexane. ^{1}H NMR ($CDCl_3$), δ (ppm): 7.96 (d, 1H), 7.86 (m, 1H), 7.54 (m, 1H), 7.33 (m, 1H), 4.68 (s, 2H).

[0414] Examples 17-30 were prepared in an analogous method to the procedure given in Example 16.

[0415] Example 17

[0416] 3-Chloromethyl-5-thiophen-3-yl-[1,2,4]oxadiazole

[0417] 3-Chloromethyl-5-thiophen-3-yl-[1,2,4]oxadiazole (197 mg, 20% yield over

2 steps, white solid) was obtained from 3-thiophenecarboxylic acid (700 mg, 4.96 mmol), EDCI (950 mg, 4.96 mmol), HOBt (670 mg, 4.96 mmol) and 2-chloro-*N*-hydroxy-acetamidine (538 mg, 5.46 mmol) in DMF (10 ml). The acyclic product was purified by flash column chromatography eluting with 2:1.2:0.8 dichloromethane:hexane:ethyl acetate. The title compound was purified by flash column chromatography using 5% ethyl acetate in hexane. ^{1}H NMR ($CDCl_3$), δ (ppm): 8.28 (s, 1H), 7.70 (d, 1H), 7.48 (m, 1H).

[0418] **Example 18**

[0419] **3-(3-Chloromethyl-[1,2,4]oxadiazol-5-yl)-5-methyl-pyridine**

[0420] 3-(3-Chloromethyl-[1,2,4]oxadiazol-5-yl)-5-methyl-pyridine (25 mg, 4% yield over 2 steps) was obtained from 5-methynicotinic acid (472 mg, 3.44 mmol), EDCI (652 mg, 3.44 mmol), HOBt (465 mg, 3.44 mmol) and 2-chloro-*N*-hydroxy-acetamidine (340 mg, 3.13 mmol) in DMF (10 ml). The acyclic intermediate was purified by flash column chromatography using 100% ethyl acetate; 200 mg (30%) of the acyclic ester was also isolated as side product.

[0421] **Example 19**

[0422] **3-Chloromethyl-5-(3-nitro-phenyl)-[1,2,4]oxadiazole**

[0423] 3-Chloromethyl-5-(3-nitro-phenyl)-[1,2,4]oxadiazole (335 mg, 30% yield over 2 steps, yellow solid) was obtained from 3-nitrobenzoic acid (847 mg, 5.07 mmol), EDCI (972 mg, 5.07 mmol), HOBt (685 mg, 5.07 mmol) and 2-chloro-*N*-hydroxy-acetamidine (500 mg, 4.61 mmol) in DMF (10 ml). The acyclic intermediate was purified by flash column chromatography using 100% ethyl acetate. Purification was performed by flash column chromatography using 15% ethyl acetate in hexane. ^{1}H NMR ($CDCl_3$), δ (ppm): 9.03 (t, 1H), 8.50 (t, 2H), 7.79 (t, 1H), 4.71 (s, 2H)

[0424] **Example 20**

[0425] **4-(3-Chloromethyl-[1,2,4]oxadiazol-5-yl)-2-methyl-pyridine**

[0426] 4-(3-Chloromethyl-[1,2,4]oxadiazol-5-yl)-2-methyl-pyridine (316 mg, 28% yield over 2 steps, yellow oil) was obtained from 6-methylpyridine-4-carboxylic acid

(800 mg, 5.8 mmol), EDCI (1.12 g, 5.8 mmol), HOBt (788 mg, 5.8 mmol) and 2-chloro-*N*-hydroxy-acetamidine (575 mg, 5.3 mmol) in DMF (10 ml) plus triethylamine (536 mg, 5.3 mmol). Purification was performed by flash column chromatography using 30% ethyl acetate in hexane. ^{1}H NMR ($CDCl_3$), δ (ppm): 8.75 (d, 1H), 7.88 (s, 1H), 7.79 (d, 1H), 4.70 (s, 2H), 2.70 (s, 3H)

[0427] Example 21

[0428] **3-Chloromethyl-5-(3-ethyl-phenyl)-[1,2,4]oxadiazole**

[0429] 3-Chloromethyl-5-(3-ethyl-phenyl)-[1,2,4]oxadiazole (446 mg, 52% yield over 2 steps, yellow oil) was obtained from 3-ethylbenzoic acid (770 mg, 3.81 mmol), EDCI (803 mg, 4.19 mmol), HOBt (566 mg, 4.19 mmol) and 2-chloro-*N*-hydroxy-acetamidine (454 mg, 4.19 mmol) in DMF (10 ml). Purification was performed by flash column chromatography using 5% ethyl acetate in hexane. ^{1}H NMR ($CDCl_3$), δ (ppm): 7.96 (t, 2H), 7.42 (m, 2H), 4.68 (s, 2H), 2.74 (m, 2H), 1.28 (m, 3H).

[0430] Example 22

[0431] **3-(3-Chloromethyl-[1,2,4]oxadiazol-5-yl)-phenyl]-dimethyl-amine**

[0432] 3-(3-Chloromethyl-[1,2,4]oxadiazol-5-yl)-phenyl]-dimethyl-amine (40 mg, 4% yield over 2 steps, yellow solid) was obtained from 3-(dimethylamino)benzoic acid (656 mg, 3.97 mmol), EDCI (761 mg, 3.97 mmol), HOBt (536 mg, 3.97 mmol) and 2-chloro-*N*-hydroxy-acetamidine (500 mg, 3.6 mmol) in DMF (10 ml). Purification was performed by flash column chromatography using 5% ethyl acetate in hexane. ^{1}H NMR ($CDCl_3$), δ (ppm): 7.46 (t, 2H), 7.37 (t, 1H), 6.94 (d, 1H), 4.68 (s, 2H), 3.04 (s, 6H).

[0433] Example 23

[0434] **3-Chloromethyl-5-(3-chloro-phenyl)-[1,2,4]oxadiazole**

[0435] 3-Chloromethyl-5-(3-chloro-phenyl)-[1,2,4]oxadiazole (406 mg, 43% yield over 2 steps, white solid) was obtained from 3-chlorobenzoic acid (708 mg, 4.52 mmol), EDCI (866 mg, 4.52 mmol), HOBt (611 mg, 4.52 mmol) and 2-chloro-*N*-hydroxy-acetamidine (446 mg, 4.11 mmol) in DMF (10 ml). Purification was

performed by flash column chromatography using 5% ethyl acetate in hexane. ^1H NMR ($CDCl_3$), δ (ppm): 8.17 (t, 1H), 8.05 (d, 1H), 7.59 (t, 1H), 7.50 (t, 1H), 4.68 (s, 2H).

[0436] Example 24

[0437] 3-Chloromethyl-5-(3-trifluoromethoxy-phenyl)-[1,2,4]oxadiazole

[0438] 3-Chloromethyl-5-(3-trifluoromethoxy-phenyl)-[1,2,4]oxadiazole (707 mg, 55% yield over 2 steps, light yellow oil) was obtained from 3-trifluoromethoxybenzoic acid (1.05 g, 5.07 mmol), EDCI (972 mg, 5.07 mmol), HOBt (685 mg, 5.07 mmol) and 2-chloro-*N*-hydroxy-acetamidine (500 mg, 4.61 mmol) in DMF (10 ml). Purification was performed by flash column chromatography using 5% ethyl acetate in hexane. ^1H NMR ($CDCl_3$), δ (ppm): 8.10 (m, 1H), 8.03 (s, 1H), 7.61 (t, 1H), 7.48 (d, 1H), 4.69 (s, 2H).

[0439] Example 25

[0440] 5-(3-Bromo-phenyl)-3-chloromethyl-[1,2,4]oxadiazole

[0441] 5-(3-Bromo-phenyl)-3-chloromethyl-[1,2,4]oxadiazole (707 mg, 55% yield over 2 steps, white solid) was obtained from 3-bromobenzoic acid (1.05 g, 5.07 mmol), EDCI (972 mg, 5.07 mmol), HOBt (685 mg, 5.07 mmol) and 2-chloro-*N*-hydroxy-acetamidine (500 mg, 4.61 mmol) in DMF (10 ml). Purification was performed by flash column chromatography using 5% ethyl acetate in hexane. 1H NMR (CDCl3) d (ppm): 8.10 (m, 1H), 8.03 (s, 1H), 7.61 (t, 1H), 7.48 (d, 1H), 4.69 (s, 2H).

[0442] Example 26

[0443] 3-Chloromethyl-5-thiophen-2-yl-[1,2,4]oxadiazole

[0444] 3-Chloromethyl-5-thiophen-2-yl-[1,2,4]oxadiazole (202 mg, 20%, off-white solid) was obtained from thiophene-2-carboxylic acid (649 mg, 5.1 mmol), 2-chloro-*N*-hydroxy-acetamidine (500 mg, 4.6 mmol), EDCI (972 mg, 5.1 mmol) and HOBt (684 mg, 5.1 mmol) in DMF (5 ml). Purification was performed by SPE (flash) chromatography using 5% ethyl acetate in hexanes. ^1H NMR ($CDCl_3$), δ (ppm): 8.00

(s, 1H), 7.83 (d, 1H), 7.19 (t, 1H), 4.13 (s, 2H).

[0445] Example 27

[0446] **3-Chloromethyl-5-(3-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazole**

[0447] 3-Chloromethyl-5-(3-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazole (312 mg, 46%, colorless oil) was obtained from 3-fluoro-5-methyl-benzoic acid (469 mg, 3.0 mmol), 2-chloro-*N*-hydroxy-acetamidine (363 mg, 3.3 mmol), EDCI (641 mg, 3.3 mmol) and HOBt (452 mg, 3.3 mmol) in DMF (5 ml). Purification was performed by SPE (flash) chromatography using 5% ethyl acetate in hexanes. ^{1}H NMR ($CDCl_3$), δ (ppm): 7.79 (s, 1H), 7.65 (d, 1H), 7.15 (d, 1H), 4.67 (s, 2H), 2.46 (s, 3H).

[0448] Example 28

[0449] **3-Chloromethyl-5-thiazol-4-yl-[1,2,4]oxadiazole**

[0450] 3-Chloromethyl-5-thiazol-4-yl-[1,2,4]oxadiazole (37 mg, 5%, yellow solid) was obtained from thiazole-4-carboxylic acid (500 mg, 3.9 mmol), 2-chloro-*N*-hydroxy-acetamidine (462 mg, 4.3 mmol), EDCI (817 mg, 4.3 mmol) and HOBt (575 mg, 4.3 mmol) in DMF (5 ml). Purification was performed by SPE (flash) chromatography using 30% ethyl acetate in hexanes. ^{1}H NMR ($CDCl_3$), δ (ppm): 9.02 (d, 1H), 8.42 (d, 1H), 4.70 (s, 2H).

[0451] Example 29

[0452] **3-Chloromethyl-5-(3-iodo-phenyl)-[1,2,4]oxadiazole**

[0453] 3-Chloromethyl-5-(3-iodo-phenyl)-[1,2,4]oxadiazole (2.9 g, 44%, white solid) was obtained from 3-iodo-benzoic acid (5.0 g, 20.2 mmol), 2-chloro-*N*-hydroxy-acetamidine (2.4 g, 22.2 mmol), EDCI (4.3 g, 22.2 mmol) and HOBt (3.0 g, 22.2 mmol) in DMF (10 ml). The acyclic ester intermediate was purified by flash column chromatography using 50–80% ethyl acetate in hexanes. The title compound was purified by SPE (flash) chromatography using 5% ethyl acetate in hexanes. ^{1}H NMR ($CDCl_3$), δ (ppm): 8.52 (s, 1H), 8.13 (d, 1H), 7.96 (d, 1H), 7.29 (t, 1H), 4.68 (s, 2H).

[0454] Example 30

[0455] **3-Chloromethyl-5-(3-methoxymethyl-phenyl)-[1,2,4]oxadiazole**

[0456] 3-Chloromethyl-5-(3-methoxymethyl-phenyl)-[1,2,4]oxadiazole (193 mg, 34%, light yellow oil) was obtained from 3-methoxymethyl-benzoic acid (395 mg, 2.4 mmol), 2-chloro-*N*-hydroxy-acetamidine (284 mg, 2.6 mmol), EDCI (501 mg, 2.6 mmol) and HOBt (353 mg, 2.6 mmol) in DMF (5 ml). Purification was performed by SPE (flash) chromatography using 5% ethyl acetate in hexanes. ^{1}H NMR ($CDCl_3$), δ (ppm): 8.14 (s, 1H), 8.08 (d, 1H), 7.61 (d, 1H), 7.53 (t, 1H), 4.68 (s, 2H), 4.54 (s, 2H), 3.44 (s, 3H).

[0457] Example 31

[0458] **5-Furan-2-yl-4-methyl-4*H*-[1,2,4]triazole-3-thiol**

[0459] 2-Furoyl chloride (0.76 ml, 7.66 mmol) was added in a dropwise manner to a solution of 4-methyl-3-thiosemicarbazide (732 mg, 6.96 mmol) and pyridine (7 ml) and the resulting solution was stirred at room temperature for 4 h. The reaction mixture was diluted with ethyl acetate (100 ml), successively washed with water (3x100 ml) and brine (100 ml). The organic phase was dried (sodium sulfate), filtered and concentrated in-vacuo. The residue was suspended in sodium bicarbonate (70 ml, 69.6 mmol, 1 M water) and left stirring at 100°C overnight. The reaction mixture was cooled to 0°C, then brought to pH about 6 using hydrochloric acid (70 ml, 1 N water). The title compound (298 mg) was collected by filtration as a white solid. ^{1}H NMR ($CDCl_3$), δ (ppm): 11.4 (bs, 1H), 7.63 (d, 1H), 7.02 (d, 1H), 6.60 (dd, 1H), 3.83 (s, 3H).

[0460] Examples 32-35 were prepared in an analogous method to the procedure given in Example 31.

[0461] Example 32

[0462] **4-Methyl-5-phenyl-4*H*-[1,2,4]triazole-3-thiol**

[0463] 4-Methyl-5-phenyl-4*H*-[1,2,4]triazole-3-thiol (478 mg, off-white solid) was obtained from 4-methyl-3-thiosemicarbazide (732 mg, 6.96 mmol) and pyridine (7

ml) with benzoyl chloride (0.89 ml, 7.66 mmol). Then sodium bicarbonate (70 ml, 69.6 mmol, 1 M water) was added at 100°C overnight and the title compound was collected by filtration. ^{1}H NMR ($CDCl_3$), δ (ppm): 12.3(bs, 1H), 7.55 (m, 5H), 3.65 (s, 3H).

[0464] **Example 33**

[0465] **4-Methyl-5-pyridin-2-yl-4*H*-[1,2,4]triazole-3-thiol**

[0466] 4-Methyl-5-pyridin-2-yl-4*H*-[1,2,4]triazole-3-thiol (44 mg, greenish solid) was obtained from 4-methyl-3-thiosemicarbazide (537 mg, 5.11 mmol) and pyridine (7 ml) with 2-pyridinecarbonyl chloride hydrochloride (1.00 g, 5.62 mmol). Then sodium bicarbonate (51 ml, 1 M water) was added at 100°C overnight and the title compound was collected using extraction and evaporation. ^{1}H NMR ($CDCl_3$), δ (ppm): 11.1 (bs, 1H), 8.70 (d, 1H), 8.02 (d, 1H), 7.84 (m, 1H), 7.41 (dd, 1H), 4.05 (s, 3H).

[0467] **Example 34**

[0468] **5-(4-Benzyl-morpholin-2-yl)-4-methyl-4H-[1,2,4]triazole-3-thiol**

[0469] (83.3 mg, dirty yellow solid) was obtained from 4-methyl-3-thiosemicarbazide (346 mg, 3.29 mmol) and pyridine (7 ml) with 4-benzyl-2-morpholinecarbonyl chloride hydrochloride (1.00 g, 3.62 mmol). Then sodium bicarbonate (33 ml, 1 M water) was added at 100°C overnight and the title compound was collected using extraction and evaporation. ^{1}H NMR ($CDCl_3$), δ (ppm): 9.48 (bs, 1H), 7.25 (m, 5H), 4.68 (dd, 1H), 3.86 (dAb, 1H), 3.68 (tAB, 1H), 3.59-3.64 (m, 5H), 3.07 (d, 1H), 2.88 (d, 1H), 2.61 (t, 1H), 2.37 (dt, 1H).

[0470] **Example 35**

[0471] **5-tert-Butyl-4-methyl-4*H*-[1,2,4]triazole-3-thiol**

[0472] 5-tert-Butyl-4-methyl-4*H*-[1,2,4]triazole-3-thiol (2.21 g, 83%, off-white solid) was obtained from 4-methyl-3-thiosemicarbazide (1.80 g, 17.2 mmol) and pyridine (20 ml) with trimethylacetyl chloride (1.92 ml, 15.6 mmol). Then sodium hydroxide (200 ml, 5% water) was added and left stirring at 60°C overnight and the

title compound was collected extraction and evaporation. ^{1}H NMR ($CDCl_3$), δ (ppm): 11.7 (bs, 1H), 3.72 (s, 3H) 1.40 (s, 9H).

[0473] Example 36

[0474] **4-Methyl-5-pyridin-3-yl-4*H*-[1,2,4]triazole-3-thiol**

[0475] A solution of 4-methyl-3-thiosemicarbazide (902 mg, 8.58 mmol), nicotinic acid (960 mg, 7.80), EDCI (1.64 g, 8.58 mmol), HOBt (1.16 g, 8.58 mmol) in DMF (10 ml) was stirred at room temperature overnight. The reaction mixture was diluted with ethyl acetate (100 ml), successively washed with hydrochloric acid (50 ml, 10% aqueous), water (50 ml), saturated sodium carbonate (50 ml, aqueous), water (50 ml) and brine (50 ml). The organic phase was dried (sodium sulfate), filtered and concentrated in-vacuo. The residue was stirred in sodium hydroxide (53.4 ml, 66.7 mmol, 5% aqueous) at 60°C overnight. The reaction mixture was cooled to room temperature, then carefully brought to pH about 6 using hydrochloric acid (1 N water). The aqueous phase was saturated with solid sodium chloride, then extracted with ethyl acetate (4x50 ml). The combined organic phase was washed with brine (100 ml), dried (sodium sulfate), filtered and concentrated in-vacuo (180 mg, off-white solid). ^{1}H NMR ($CDCl_3$), δ (ppm): 11.6 (bs, 1H), 8.94 (s, 1H), 8.83 (dd, 1H), 7.98 (m, 1H), 7.51 (dd, 1H), 3.69 (s, 3H).

[0476] Examples 37-39 were prepared in an analogous method to the procedure given in Example 36.

[0477] Example 37

[0478] **4-Methyl-5-thiophene-3-yl-4*H*-[1,2,4]triazole-3-thiol**

[0479] 4-Methyl-5-thiophene-3-yl-4*H*-[1,2,4]triazole-3-thiol (693 mg, white solid) was obtained from 4-methyl-3-thiosemicarbazide (902 mg, 8.58 mmol), 3-thiophenecarboxylic acid (1 g, 7.80 mmol), EDCI (1.64 g, 8.58 mmol), HOBt (1.16 g, 8.58 mmol) in DMF (10 ml). Then sodium hydroxide (88 ml, 110 mmol, 5% aqueous) at 60°C overnight and the title compound was product collected extraction and evaporation. ^{1}H NMR ($CDCl_3$), δ (ppm): 11.4 (bs, 1H), 7.77 (dd, 1H), 7.51 (dd, 1H),

7.42 (dd, 1H), 3.61 (s, 3H).

[0480] Example 38

[0481] **4-Methyl-5-thiazol-4-yl-4*H*-[1,2,4]triazole-3-thiol**

[0482] 4-Methyl-5-thiazol-4-yl-4*H*-[1,2,4]triazole-3-thiol (71.2 mg, sticky yellow oil) was obtained from 4-methyl-3-thiosemicarbazide (902 mg, 8.58 mmol), 4-carboxythiazole (1.01 g, 7.80), EDCI (1.64 g, 8.58 mmol), HOBt (1.16 g, 8.58 mmol) in DMF (10 ml). Then sodium hydroxide (43 ml, 54 mmol, 5% aqueous) at 60°C overnight and the title compound was collected extraction and evaporation.

[0483] Example 39

[0484] **5-Cyclohexyl-4-methyl-4*H*-[1,2,4]triazole-3-thiol**

[0485] 5-Cyclohexyl-4-methyl-4*H*-[1,2,4]triazole-3-thiol (403 mg, beige solid) was obtained from 4-methyl-3-thiosemicarbazide (1.80 g, 17.2 mmol), cyclohexane carboxylic acid (2 g, 15.6 mmol), EDCI (2.99 g, 17.2 mmol) and HOBt (2.10 g, 17.2 mmol) in DMF(20 ml); then sodium hydroxide (195 ml, 244 mmol, 5% aqueous) at 60°C overnight.

[0486] Example 40

[0487] **2-[5-(3-Methoxy-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1*H*-benzoimidazole**

[0488] 1*H*-Benzoimidazole-2-thiol (150 mg, 1 mmol) was added to a solution of the 3-chloromethyl-5-(3-methoxy-phenyl)-[1,2,4]oxadiazole (30 mg, 0.13 mmol) and potassium carbonate (50 mg, 0.36 mmol) in DMF (2 ml) at room temperature. The solvent was removed in vacuo and the product obtained by flash chromatography using 20-100% ethyl acetate in hexane. ^{1}H NMR ($CDCl_3$), δ (ppm): 7.71 (d, 1H), 7.62 (d, 1H), 7.53 (m, 2H), 7.42 (t, 1H), 7.18 (overlapping , m, 3H), 4.52 (s, 2H), 3.87 (s, 3H).

Examples 41-92 were prepared in an analogous method to the procedure given in Example 40.

[0489] **Example 41**

[0490] **5-(3-Methoxy-phenyl)-3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole**

[0491] The title compound was prepared from 3-chloromethyl-5-(3-methoxy-phenyl)-[1,2,4]oxadiazole (50 mg, 0.22 mmol), potassium carbonate (92.4 mg, 0.67 mmol), 4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazole-3-thiol (52.8 mg, 0.27 mmol) in acetonitrile (1 ml) at room temperature. Purification was performed by SPE (flash) chromatography using 30-40% ethyl acetate in hexanes afforded 76 mg (90%) of the title compound as a white solid. ^{1}H NMR ($CDCl_3$), δ (ppm): 7.68 (d, 1H), 7.57 (t, 1H), 7.49 (m, 2H), 7.41 (t, 1H), 7.15 (m, 2H), 4.53 (s, 2H), 3.85 (s, 3H), 3.72 (s, 3H). LC-MS $(M+1)^+$ 386.3.

[0492] **Example 42**

[0493] **3-[5-(1-Methyl-5-thiophen-2-yl-1*H*-imidazol-2-ylsulfanylmethyl)-[1,2,4]oxadiazol-3-yl]-benzonitrile**

[0494] 3-[5-(1-Methyl-5-thiophen-2-yl-1*H*-imidazol-2-ylsulfanylmethyl)-[1,2,4]oxadiazol-3-yl]-benzonitrile (39 mg, 47%, white solid) was obtained from 3-chloromethyl-3-(5-chloromethyl-[1,2,4]oxadiazol-3-yl)-benzonitrile (50 mg, 0.22 mmol), potassium carbonate (92.4 mg, 0.67 mmol), 4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazole-3-thiol (52.8 mg, 0.27 mmol) in acetonitrile (1 ml) at room temperature. Purification was performed by SPE (flash) chromatography using 50-70% ethyl acetate in hexanes. ^{1}H NMR ($CDCl_3$), δ (ppm): 8.34 (s, 1H), 8.28 (d, 1H), 7.79 (d, 1H), 7.60 (t, 1H), 7.53 (d, 1H), 7.49 (d, 1H), 7.19 (m, 1H), 4.70 (s, 2H), 3.74 (s, 3H). LS-MS (ES+full scan, $C_{17}H_{12}N_6OS_2$) M^+ calc. 380.05, found $(M+1)^+$ 381.04.

[0495] **Example 43**

[0496] **3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]traiazol-3-ylsulfanylmethyl)-5-phenyl-[1,2,4]oxadiazole**

[0497] 3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]traiazol-3-ylsulfanylmethyl)-5-phenyl-[1,2,4]oxadiazole (41.2 mg, 44%, off-white solid) was obtained from 3-

chloromethyl-5-phenyl-[1,2,4]oxadiazole (50 mg, 0.26 mmol), potassium carbonate (106 mg, 0.77 mmol), 4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazole-3-thiol (60.8 mg, 0.31 mmol) in acetonitrile (2 ml) at 60°C overnight. Purification was performed on silica gel using 50% ethyl acetate in hexanes. ^{1}H NMR ($CDCl_3$), δ (ppm): 8.09 (m, 2H), 7.57 (m, 5H), 7.17 (dd, 1H), 4.53 (s, 2H), 3.72 (s, 3H).

[0498] Example 44

[0499] 2-[5-(3-Methoxy-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-5-methyl-1*H*-benzoimidazole

[0500] 2-[5-(3-Methoxy-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-5-methyl-1*H*-benzoimidazole (75.5 mg, 70.5%, white foam) was obtained from 3-chloromethyl-5-(3-methoxy-phenyl)-[1,2,4]oxadiazole (82 mg, 0.365 mmol), potassium carbonate (210 mg, 1.520 mmol), 2-thiol-5-methyl-1H-benzoimidazole (50 mg, 0.305 mmol) in acetonitrile (3 ml) at room temperature. Purification was performed by SPE flash chromatography using 50% ethyl acetate in hexanes followed by trituration with ethyl acetate. ^{1}H NMR ($CDCl_3$), δ (ppm): 11.95 (bs, 1H), 7.80 (d, 1H), 7.70 (s, 1H), 7.52 (m, 2H), 7.21 (dd, 2H), 7.17 (d, 1H), 4.40 (s, 2H), 3.95 (s, 3H), 2.50 (s, 3H).

[0501] Example 45

[0502] 3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole

[0503] 3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole (76 mg, 85%, white solid) was obtained from 3-chloromethyl-5-m-tolyl-[1,2,4]oxadiazole (50 mg, 0.24 mmol), potassium carbonate (99.4 mg, 0.72 mmol), 4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazole-3-thiol (56.7 mg, 0.27 mmol) in acetonitrile (1 ml) at room temperature. Purification was performed by SPE (flash) chromatography using 50-70% ethyl acetate in hexanes. ^{1}H NMR ($CDCl_3$), δ (ppm): 7.89 (m, 2H), 7.50 (m, 2H), 7.40 (m, 2H), 7.18 (t, 1H), 4.52 (s, 2H), 3.71 (s, 3H), 2.41 (s, 3H).

[0504] Example 46

[0505] 3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-trifluoromethyl-phenyl)-[1,2,4]oxadiazole

[0506] 3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-trifluoromethyl-phenyl)-[1,2,4]oxadiazole (84 mg, 86%, white solid) was obtained from 3-chloromethyl-5-(3-trifluoromethyl-phenyl)-[1,2,4]oxadiazole (60 mg, 0.23 mmol), potassium carbonate (95 mg, 0.69 mmol), 4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazole-3-thiol (54 mg, 0.27 mmol) in acetonitrile (1 ml) at room temperature. Purification was performed by SPE (flash) chromatography using 40-60% ethyl acetate in hexanes. ^{1}H NMR ($CDCl_3$), δ (ppm): 8.38 (s, 1H), 7.29 (d, 1H), 7.86 (d, 1H), 7.68 (t, 1H), 7.50 (t, 2H), 7.19 (m, 1H), 4.57 (s, 2H), 3.75 (s, 3H).

[0507] Example 47

[0508] 3-(3-Methoxy-phenyl)-5-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole

[0509] 3-(3-Methoxy-phenyl)-5-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole (74.3 mg, 88%, white solid) was obtained from 4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazole-3-thiol (53.3 mg, 0.27 mmol), 5-chloromethyl-3-(3-methoxy-phenyl)-[1,2,4]oxadiazole (50 mg, 0.22) mmol), and potassium carbonate (92.6 mg, 0.67 mmol) in acetonitrile (1 ml) at room temperature. Purification was performed by SPE (flash) chromatography using 40-70% ethyl acetate in hexane. ^{1}H NMR ($CDCl_3$), δ (ppm): 7.62 (d, 1H), 7.52 (d, 2H), 7.48 (d, 1H), 7.37 (t, 1H), 7.18 (t, 1H), 7.06 (m, 1H), 4.64 (s, 2H), 3.84 (s, 3H), 3.71 (s, 3H). LC-MS (MH+): 386.06.

[0510] Example 48

[0511] 5-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-3-phenyl-[1,2,4]oxadiazole

[0512] 5-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-3-phenyl-[1,2,4]oxadiazole (79.9 mg, 87%, white solid) was obtained from 4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazole-3-thiol (86.8 mg, 0.44 mmol), 5-chloromethyl-3-

phenyl-[1,2,4]oxadiazole (50 mg, 0.26 mmol), and potassium carbonate (152.0 mg, 1.1 mmol) in acetonitrile (1 ml) at room temperature. Purification was performed by SPE (flash) chromatography using 40-70% ethyl acetate in hexane. ^{1}H NMR ($CDCl_3$), δ (ppm): 8.02 (d, 2H), 7.47 (m, 5H), 7.18 (t, 1H).

[0513] Example 49

[0514] 5-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-3-m-tolyl-[1,2,4]oxadiazole

[0515] 5-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-3-m-tolyl-[1,2,4]oxadiazole (71.8 mg, 91%, white solid) was obtained from 4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazole-3-thiol (78.9 mg, 0.40 mmol), 5-chloromethyl-3-m-tolyl-[1,2,4]oxadiazole (50 mg, 0.24 mmol) and potassium carbonate (138.2 mg, 1.0 mmol) in acetonitrile (1 ml) at room temperature. Purification was performed by SPE (flash) chromatography using 45-65% ethyl acetate in hexane. ^{1}H NMR ($CDCl_3$), δ (ppm): 7.82 (d, 2H), 7.52 (d, 1H), 7.47 (d, 1H), 7.31 (m, 2H), 7.18 (m, 1H), 4.64 (s, 2H), 3.70 (s, 3H), 2.39 (s, 3H). LC-MS (MH^+): 370.06.

[0516] Example 50

[0517] 3-[3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzonitrile

[0518] 3-[3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzonitrile (130 mg, 75%) was obtained from 3-(3-chloromethyl-[1,2,4]oxadiazol-5-yl)-benzonitrile (100 mg, 0.45 mmol) with K_2CO_3 (189 mg, 1.36 mmol) and 4-methyl-5-(2-thienyl)1,2,4-triazole-3-thiol (110 mg, 0.54 mmol) in acetonitrile at room temperature. Purification was performed by flash chromatography using 50% ethyl acetate in dichloromethane. ^{1}H NMR ($CDCl_3$), δ (ppm): 8.38 (bs,1H), 8.32 (d,1H), 7.88 (d,1H), 7.68 (t,1H), 7.51 (dd, 2H), 7.18 (dd,1H), 4.56 (s,2H), 3.75 (s,3H); LC-MS $(M+H)^+$: 381.

[0519] Example 51

[0520] 3-[4-Methyl-5-(2-methyl-thiazol-4-yl)-4*H*-[1,2,4]triazol-3-

ylsulfanylmethyl]-5-m-tolyl-[1,2,4]oxadiazole

[0521] 3-[4-Methyl-5-(2-methyl-thiazol-4-yl)-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl]-5-m-tolyl-[1,2,4]oxadiazole (82.8 mg, 90%, white solid) was obtained from 3-chloromethyl-5-m-tolyl-[1,2,4]oxadiazole (50 mg, 0.24 mmol), potassium carbonate (99 mg, 0.72 mmol), 4-methyl-5-(2-methyl-thiazol-4-yl)-4H-[1,2,4]triazole-3-thiol (61 mg, 0.29 mmol) in acetonitrile (2 ml) at 60°C overnight. Purification was performed on silica gel using 80% ethyl acetate in hexanes. ^{1}H NMR ($CDCl_3$), δ (ppm): 7.96 (s, 1H), 7.88 (m, 2H), 7.38 (m, 2H), 4.53 (s, 2H), 3.91 (s, 3H), 2.75 (s, 3H), 2.41 (s, 3H).

[0522] Example 52

[0523] **3-[5-(2-Methyl-thiazol-4-yl)-[1,3,4]oxadiazol-2-ylsulfanylmethyl]-5-m-tolyl-[1,2,4]oxadiazole**

[0524] 3-[5-(2-Methyl-thiazol-4-yl)-[1,3,4]oxadiazol-2-ylsulfanylmethyl]-5-m-tolyl-[1,2,4]oxadiazole (89 mg, 99%, off-white solid) was obtained from 3-chloromethyl-5-m-tolyl-[1,2,4]oxadiazole (50 mg, 0.24 mmol), potassium carbonate (99 mg, 0.72 mmol), 5-(2-methyl-thiazol-4-yl)-[1,3,4]oxadiazole-2-thiol (57.3 mg, 0.29 mmol) in acetonitrile (2 ml) at 60°C overnight. Purification was performed on silica gel using 80% ethyl acetate in hexanes. ^{1}H NMR ($CDCl_3$), δ (ppm): 7.97 (s, 1H), 7.90 (m, 2H), 7.40 (m, 2H), 4.66 (s, 2H), 2.80 (s, 3H), 2.42 (s, 3H).

[0525] Example 53

[0526] **3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-2-yl-[1,2,4]oxadiazole**

[0527] 3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-2-yl-[1,2,4]oxadiazole (80 mg, 88%, white solid) was obtained from 3-chloromethyl-5-thiophen-2-yl-[1,2,4]oxadiazole (50 mg, 0.25 mmol), potassium carbonate (103 mg, 0.75 mmol), 4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazole-3-thiol (59 mg, 0.30 mmol) in acetonitrile (1 ml) at room temperature. Purification was performed by SPE (flash) chromatography using 50-70% ethyl acetate in hexanes. ^{1}H NMR ($CDCl_3$), δ (ppm): 7.89 (d, 1H), 7.65 (m, 1H), 7.51 (m, 2H), 7.19 (m, 2H), 4.50

(t, 2H), 3.74 (s, 3H).

[0528] Example 54

[0529] 3-[5-(2,4-Dimethyl-thiazol-5-yl)-4-methyl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl]-5-m-tolyl-[1,2,4]oxadiazole

[0530] 3-[5-(2,4-Dimethyl-thiazol-5-yl)-4-methyl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl]-5-m-tolyl-[1,2,4]oxadiazole (54.2 mg, 57%, off-white solid) was obtained from 3-chloromethyl-5-m-tolyl-[1,2,4]oxadiazole (50 mg, 0.24 mmol), potassium carbonate (99 mg, 0.72 mmol), 5-(2,4-dimethyl-thiazol-5-yl)-4-methyl-4H-[1,2,4]triazole-3-thiol (65.1 mg, 0.29 mmol) in acetonitrile (2 ml) at 60°C overnight. Purification was performed on silica gel using 80% ethyl acetate in hexanes. ^{1}H NMR ($CDCl_3$), δ (ppm):: 7.88 (m, 2H), 7.39 (m, 2H), 4.57 (s, 2H), 3.49 (s, 3H), 2.73 (s, 3H), 2.43 (d, 6H).

[0531] Example 55

[0532] 3-[4-Methyl-5-(5-nitro-furan-2-yl)-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl]-5-m-tolyl-[1,2,4]oxadiazole

[0533] 3-[4-Methyl-5-(5-nitro-furan-2-yl)-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl]-5-m-tolyl-[1,2,4]oxadiazole (77.9 mg, 81%, yellow solid) was obtained from 3-chloromethyl-5-m-tolyl-[1,2,4]oxadiazole (50 mg, 0.24 mmol), potassium carbonate (99 mg, 0.72 mmol), 4-methyl-5-(5-nitro-furan-2-yl)-4H-[1,2,4]triazole-3-thiol (65.1 mg, 0.29 mmol) in acetonitrile (2 ml) at 60°C overnight. Purification was performed on silica gel using 80% ethyl acetate in. ^{1}H NMR ($CDCl_3$), δ (ppm): 7.90 (m, 2H), 7.46 (d, 1H), 7.40 (m, 2H), 7.33 (d, 1H), 4.59 (s, 2H), 3.91 (s, 3H), 2.42 (s, 3H).

[0534] Example 56

[0535] 4-[4-Methyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4*H*-[1,2,4]triazol-3-yl]-pyridine

[0536] 4-[4-Methyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4*H*-[1,2,4]triazol-3-yl]-pyridine (66 mg, 75%, white solid) was obtained from 3-chloromethyl-5-m-tolyl-[1,2,4]oxadiazole (50 mg, 0.24 mmol), potassium carbonate

(99 mg, 0.72 mmol), 4-methyl-5-pyridin-4-yl-4H-[1,2,4]triazole-3-thiol (55.3 mg, 0.29 mmol) in acetonitrile (2 ml) at 60°C overnight. Purification was performed on silica gel using 80% ethyl acetate in hexanes. ^{1}H NMR ($CDCl_3$), δ (ppm): 8.79 (dd, 2H), 7.89 (m, 2H), 7.63 (dd, 2H), 7.40 (m, 2H), 4.59 (s, 2H), 3.69 (s, 3H), 2.41 (s, 3H).

[0537] Example 57

[0538] 3-[5-(4-tert-Butyl-phenyl)-4-methyl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl]-5-m-tolyl-[1,2,4]-oxadiazole

[0539] 3-[5-(4-tert-Butyl-phenyl)-4-methyl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl]-5-m-tolyl-[1,2,4]-oxadiazole (100 mg, 99%, white waxy solid) was obtained from 3-chloromethyl-5-m-tolyl-[1,2,4]oxadiazole (50 mg, 0.24 mmol), potassium carbonate (99 mg, 0.72 mmol), 5-(4-tert-butyl-phenyl)-4-methyl-4*H*-[1,2,4]triazole-3-thiol (71.1 mg, 0.29 mmol) in acetonitrile (2 ml) at 60°C overnight. Purification was performed on silica gel using 80% ethyl acetate in hexanes. ^{1}H NMR ($CDCl_3$), δ (ppm): 7.89 (m, 2H), 7.57 (m, 4H), 7.39 (d, 2H), 4.55 (s, 2H), 3.61 (s, 3H), 2.40 (s, 3H), 1.35 (s, 9H).

[0540] Example 58

[0541] 2-Chloro-5-[4-methyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4*H*-[1,2,4]triazol-3-yl]-pyridine

[0542] 2-Chloro-5-[4-methyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4*H*-[1,2,4]triazol-3-yl]-pyridine (53.8 mg, 56%, white solid) was obtained from 3-chloromethyl-5-m-tolyl-[1,2,4]oxadiazole (50 mg, 0.24 mmol), potassium carbonate (99 mg, 0.72 mmol), 5-(6-chloro-pyridin-3-yl)-4-methyl-4H-[1,2,4]triazole-3-thiol (65.2 mg, 0.29 mmol) in acetonitrile (2 ml) at 60°C overnight. Purification was performed on silica gel using 80% ethyl acetate in hexanes. ^{1}H NMR ($CDCl_3$), δ (ppm): 8.67 (d, 1H), 8.02 (dd, 1H), 7.88 (m, 2H), 7.49 (d, 1H), 7.40 (m, 2H), 4.58 (s, 2H), 3.65 (s, 3H), 2.42 (s, 3H).

Example 59

[0543] 2-[5-(3-Methoxy-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-

benzooxazole

[0544] 2-[5-(3-Methoxy-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-benzooxazole (138 mg, 62%) was obtained from 3-chloromethyl-5-(3-methoxy-phenyl)-[1,2,4]oxadiazole (225.9 mg, 1.11 mmol), benzooxazole-2-thiol (167 mg, 1.00 mmol), potassium carbonate (180 mg, 1.3 mmol) in DMF (4.5 ml) at room temperature overnight. Purification was performed on silica gel using 10-20% ethyl acetate in hexanes. ^{1}H NMR ($CDCl_3$), δ (ppm):: 7.67 (d, 1H), 7.57 (m, 3H), 7.43 (t, 1H), 7.21 (m, 2H), 7.14 (m, 1H), 4.50 (s, 2H), 3.86 (s, 3H).

[0545] Example 60

[0546] 3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-3-yl-[1,2,4]oxadiazole

[0547] 3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-3-yl-[1,2,4]oxadiazole (73.6 mg, 73%, white solid) was obtained from 4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazole-3-thiol (61 mg, 0.31 mmol), 3-chloromethyl-5-thiophen-3-yl-[1,2,4]oxadiazole (50 mg, 0.28 mmol), and potassium carbonate (115 mg, 0.83 mmol) in acetonitrile (1 ml) at room temperature. Purification was performed by SPE (flash) chromatography using 50-70% ethyl acetate in hexane. ^{1}H NMR ($CDCl_3$), δ (ppm): 8.20 (d, 1H), 7.64 (d, 1H), 7,48 (m, 3H), 7.18 (m, 1H), 4.52 (s, 2H), 3.72 (s, 3H)

[0548] Example 61

[0549] 3-(5-Furan-2-yl-4-methyl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole

[0550] 3-(5-Furan-2-yl-4-methyl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole (51.0 mg, 76%, white solid) was obtained from 3-chloromethyl-5-m-tolyl-[1,2,4]oxadiazole (40.0 mg, 0.19 mmol), potassium carbonate (79 mg, 0.58 mmol), 5-furan-2-yl-4-methyl-4H-[1,2,4]triazole-3-thiol (41.7 mg, 0.23 mmol) in acetonitrile (2 ml) at 60°C overnight. Purification was performed on silica gel using 80% ethyl acetate in hexanes. ^{1}H NMR ($CDCl_3$), δ (ppm): 7.88 (m, 2H), 7.58 (s, 1H), 7.40 (m, 2H), 7.10 (d, 1H), 6.58 (dd, 1H), 4.51 (s, 2H), 3.77 (s, 3H), 2.41 (s, 3H).

[0551] Example 62

[0552] 5-(3-Fluoro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole

[0553] 5-(3-Fluoro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole (75.4 mg, 83%, white solid) was obtained from 4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazole-3-thiol (51 mg, 0.26 mmol), 3-chloromethyl-5-(3-fluoro-phenyl)-[1,2,4]oxadiazole (50 mg, 0.24 mmol) and potassium carbonate (98 mg, 0.71 mmol) in acetonitrile (1 ml) at room temperature. Purification was performed by SPE (flash) chromatography using 55-60% ethyl acetate in hexane. ^{1}H NMR ($CDCl_3$), δ (ppm): 7.89 (d, 1H), 7.78 (m, 1H), 7.51 (m, 3H), 7.32 (m, 1H), 7.18 (m, 1H), 4.55 (s, 2H), 3.74 (s, 3H)

[0554] Example 63

[0555] 2-(5-m-Tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-pyridine

[0556] 2-(5-m-Tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-pyridine (27.3 mg, 96.5%) was obtained from 3-chloromethyl-5-m-tolyl-[1,2,4]oxadiazole (20.8 mg, 0.1 mmol) with pyridine-2-thiol (12.2 mg, 0.11 mmol) and potassium carbonate in DMF (0.8 ml) at room temperature for 15 h. Purification was performed by flash chromatography on silica gel using 20% ethyl acetate in hexane. ^{1}H NMR ($CDCl_3$), δ (ppm): 8.47 (dd, 1H), 7.94 (s, 1H), 7.90 (t, 1H), 7.51 (dt, 1H), 7.38 (d, 2H), 7.26 (dd, 1H), 7.02 (dd, 1H), 4.61 (s, 2H), 2.42 (s, 3H).

[0557] Example 64

[0558] 2-[5-(3-Methoxy-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1*H*-imidazo[4,5-b]pyridine

[0559] 2-[5-(3-Methoxy-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1*H*-imidazo[4,5-b]pyridine (74.5 mg, 96%) was obtained from 3-chloromethyl-5-(3-methoxy-phenyl)-[1,2,4]oxadiazole (51.2 mg, 0.25 mmol), 1*H*-imidazo[4,5-b]pyridine-2-thiol (37.5 mg, 0.23 mmol) and potassium carbonate (80 mg, 0.58 mmol) in DMF (1.5 ml) at room temperature overnight. Purification was performed on silica

gel using 25-50% ethyl acetate in dichloromethane. ^{1}H-NMR (DMSO-d_6), δ (ppm): 8.24 (br s, 1H), 7.88 br s, 1H), 7.66 (d, 1H), 7.55 (m, 3H), 7.29 (d, 1H), 7.19 (m, 1H), 4.82 (s, 2H), 3.85 (s, 3H).

[0560] Example 65

[0561] 5-(3-Fluoro-5-methyl-phenyl)-3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole

[0562] 5-(3-Fluoro-5-methyl-phenyl)-3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole (58 mg, 68%, white solid) was obtained from 3-chloromethyl-5-(3-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazole (50 mg, 0.22 mmol), potassium carbonate (91.5 mg, 0.66 mmol), 4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazole-3-thiol (52.2 mg, 0.26 mmol) in acetonitrile (1 ml) at room temperature. Purification was performed by SPE (flash) chromatography using 40-100% ethyl acetate in hexanes. ^{1}H NMR ($CDCl_3$), δ (ppm): 7.70 (s, 1H), 7.58 (d, 1H), 7.52 (m, 1H), 7.49 (m, 1H), 7.18 (m, 1H), 7.12 (d, 1H), 4.53 (s, 2H), 3.73 (s, 3H), 2.42 (s, 3H).

[0563] Example 66

[0564] 3-Methyl-5-[3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine

[0565] 3-Methyl-5-[3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine (19.0 mg, 43%, light yellow solid) was obtained from 4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazole-3-thiol (26 mg, 0.13 mmol), 3-(3-chloromethyl-[1,2,4]oxadiazol-5-yl)-5-methyl-pyridine (25 mg, 0.12 mmol) and potassium carbonate (50 mg, 0.36 mmol) in acetonitrile (1 ml) at room temperature. Purification was performed by SPE (flash) chromatography using 100% ethyl acetate. ^{1}H NMR ($CDCl_3$), δ (ppm): 9.13 (s, 1H), 8.65 (s, 1H), 8.16 (s, 1H), 7.50 (m, 2H), 7.19 (t, 1H) 4.57 (s, 2H), 3.74 (s, 3H), 2.43 (s, 3H)

[0566] Example 67

[0567] 3-(4-Methyl-5-phenyl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-

[1,2,4]oxadiazole

[0568] 3-(4-Methyl-5-phenyl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole (55.8 mg, 67%, white solid) was obtained from 3-chloromethyl-5-m-tolyl-[1,2,4]oxadiazole (48.4 mg, 0.23 mmol), potassium carbonate (96 mg, 0.70 mmol), 4-methyl-5-phenyl-4*H*-[1,2,4]triazole-3-thiol (44.4 mg, 0.23 mmol) in acetonitrile (2 ml) at 60°C overnight. Purification was performed on silica gel using 50% ethyl acetate in hexanes. ^{1}H NMR ($CDCl_3$), δ (ppm): 7.89 (m, 2H), 7.64 (m, 2H), 7.50 (m, 3H), 7.39 (m, 2H), 4.56 (s, 2H), 3.61 (s, 3H), 2.41 (s, 3H).

[0569] Example 68

[0570] 2-[4-Methyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4*H*-[1,2,4]triazol-3-yl]-pyridine

[0571] 2-[4-Methyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4*H*-[1,2,4]triazol-3-yl]-pyridine (42.8 mg, 51%, off-white solid) was obtained from 3-chloromethyl-5-m-tolyl-[1,2,4]oxadiazole (48.4 mg, 0.23 mmol), potassium carbonate (96 mg, 0.70 mmol), 4-methyl-5-pyridin-2-yl-4*H*-[1,2,4]triazole-3-thiol (44.6 mg, 0.23 mmol) in acetonitrile (2 ml) at 60°C overnight. Purification was performed on silica gel using 50% ethyl acetate in hexanes. ^{1}H NMR ($CDCl_3$), δ (ppm): 8.62 (d, 1H), 8.30 (d, 1H), 7.85 (m, 3H), 7.36 (m, 3H), 4.59 (s, 2H), 4.02 (s, 3H), 2.40 (s, 3H).

[0572] Example 69

[0573] 4-Benzyl-2-[4-methyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4*H*-[1,2,4]triazol-3-yl]-morpholine

[0574] 4-Benzyl-2-[4-methyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4*H*-[1,2,4]triazol-3-yl]-morpholine (95.8 mg, 83%, clear oil) was obtained from 3-chloromethyl-5-m-tolyl-[1,2,4]oxadiazole (59.9 mg, 0.29 mmol), potassium carbonate (119 mg, 0.86 mmol), 5-(4-benzyl-morpholin-2-yl)-4-methyl-4*H*-[1,2,4]triazole-3-thiol (83.3 mg, 0.29 mmol) in acetonitrile (2 ml) at 60°C overnight. Purification was performed on silica gel using 10% methanol in ethyl acetate. ^{1}H NMR ($CDCl_3$), δ (ppm): 7.88 (m, 2H), 7.31 (m, 7H), 4.75 (dd, 1H), 4.47 (dd, 2H), 3.84 (m, 2H), 3.59 (bs, 5H), 3.20 (d, 1H), 2.72 (m, 2H), 2.43 (s, 3H), 2.30 (dt, 1H).

[0575] Example 70

[0576] 4-[4-Methyl-5-(5-thiophen-3-yl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4*H*-[1,2,4]triazol-3-yl]-pyridine

[0577] 4-[4-Methyl-5-(5-thiophen-3-yl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4*H*-[1,2,4]triazol-3-yl]-pyridine (24 mg, 34%, white solid) was obtained from 3-chloromethyl-5-thiophen-3-yl-[1,2,4]oxadiazole (40 mg, 0.20 mmol), potassium carbonate (82.5 mg, 0.60 mmol), 4-methyl-5-pyridin-4-yl-4*H*-[1,2,4]triazole-3-thiol (38.3 mg, 0.20 mmol) in acetonitrile (2 ml) at 60°C overnight. Purification was performed on silica gel using 10% methanol in ethyl acetate. ^{1}H NMR ($CDCl_3$), δ (ppm): 8.80 (bs, 2H), 8.20 (dd, 1H), 7.62 (m, 3H), 7.45 (dd, 1H), 4.59 (s, 2H), 3.70 (s, 3H).

[0578] Example 71

[0579] 3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiazol-4-yl-[1,2,4]oxadiazole

[0580] 3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiazol-4-yl-[1,2,4]oxadiazole (44 mg, 67%, white solid) was obtained from 3-chloromethyl-5-thiophen-2-yl-[1,2,4]oxadiazole (37 mg, 0.18 mmol), potassium carbonate (75.3 mg, 0.54 mmol), 4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazole-3-thiol (43 mg, 0.22 mmol) in acetonitrile (1 ml) at room temperature. Purification was performed by SPE (flash) chromatography using 50-100% ethyl acetate in hexanes. ^{1}H NMR (DMSO), δ (ppm): 9.37 (d, 1H), 8.86 (d, 1H), 7.80 (d, 1H), 7.65 (d, 1H), 7.26 (t, 1H), 4.54 (s, 2H), 3.75 (s, 3H).

[0581] Example 72

[0582] 3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-nitro-phenyl)-[1,2,4]oxadiazole

[0583] 3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-nitro-phenyl)-[1,2,4]oxadiazole (21.1 mg, 13%, white solid) was obtained from 4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazole-3-thiol (91 mg, 0.46 mmol), 3-

chloromethyl-5-(3-nitro-phenyl)-[1,2,4]oxadiazole (100 mg, 0.42 mmol) and and potassium carbonate (173 mg, 1.25 mmol) in acetonitrile (2 ml) at room temperature. Purification was performed by SPE (flash) chromatography using 60% ethyl acetate in hexane. ^{1}H NMR ($CDCl_3$), δ (ppm): 8.96 (s, 1H), 8.44 (t, 2H), 7.75 (t, 1H), 7.51 (m, 2H), 7.19 (t, 1H), 4.59 (s, 2H), 3.76 (s, 3H)

[0584] Example 73

[0585] 2-Methyl-4-[3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine

[0586] 2-Methyl-4-[3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine (59.2 mg, 66%, white solid) was obtained from 4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazole-3-thiol (51 mg, 0.26 mmol), 4-(3-chloromethyl-[1,2,4]oxadiazol-5-yl)-2-methyl-pyridine (50 mg, 0.24 mmol), and potassium carbonate (100 mg, 0.72 mmol) in acetonitrile (1 ml) at room temperature. Purification was performed by SPE (flash) chromatography using 100% ethyl acetate. ^{1}H NMR ($CDCl_3$), δ (ppm): 8.71 (d, 1H), 7.79 (s, 1H), 7.73 (d, 1H), 7.49 (m, 2H), 7.19 (t, 1H), 4.58 (s, 2H), 3.73 (s, 3H), 2.65 (s, 3H)

[0587] Example 74

[0588] 3-[4-Methyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine

[0589] 3-[4-Methyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine (30 mg, off-white solid) was obtained from 3-chloromethyl-5-m-tolyl-[1,2,4]oxadiazole (50 mg, 0.24 mmol), potassium carbonate (100 mg, 0.72 mmol), 4-methyl-5-pyridin-3-yl-4H-[1,2,4]triazole-3-thiol (46.1 mg, 0.24 mmol) in acetonitrile (2 ml) at 60°C overnight. Purification was performed on silica gel using 5% methanol in ethyl acetate. ^{1}H NMR ($CDCl_3$), δ (ppm): 8.90 (bs, 1H), 8.76 (bs, 1H), 8.03 (m, 1H), 7.88 (m, 2H), 7.46 (dd, 1H), 7.40 (m, 2H), 4.58 (s, 2H), 3.66 (s, 3H), 2.42 (s, 3H).

[0590] Example 75

[0591] 3-(4-Methyl-5-thiophene-3-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole

[0592] 3-(4-Methyl-5-thiophene-3-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole (60 mg, white solid) was obtained from 3-chloromethyl-5-m-tolyl-[1,2,4]oxadiazole (50 mg, 0.24 mmol), potassium carbonate (100 mg, 0.72 mmol), 4-methyl-5-thiophene-3-yl-4*H*-[1,2,4]triazole-3-thiol (47.3 mg, 0.24 mmol) in acetonitrile (2 ml) at 60°C overnight. Purification was performed on silica gel using 40% ethyl acetate in dichloromethane. ^{1}H NMR ($CDCl_3$), δ (ppm): 7.87 (m, 2H), 7.71 (dd, 1H), 7.48 (m, 2H), 7.38 (m, 2H), 4.52 (s, 2H), 3.67 (s, 3H), 2.41 (s, 3H).

[0593] Example 76

[0594] 3-(4-Methyl-5-thiazol-4-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole

[0595] 3-(4-Methyl-5-thiazol-4-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole (30 mg, off-white solid) was obtained from 3-chloromethyl-5-m-tolyl-[1,2,4]oxadiazole (50 mg, 0.24 mmol), potassium carbonate (100 mg, 0.72 mmol), 4-methyl-5-thiazol-4-yl-4*H*-[1,2,4]triazole-3-thiol (47.5 mg, 0.24 mmol) in acetonitrile (2 ml) at 60°C overnight. Purification was performed on silica gel using 60% ethyl acetate in dichloromethane. ^{1}H NMR ($CDCl_3$), δ (ppm): 8.89 (d, 1H), 8.22 (d, 1H), 7.88 (m, 2H), 7.38 (m, 2H), 4.55 (s, 2H), 3.94 (s, 3H), 2.41 (s, 3H).

[0596] Example 77

[0597] 5-(3-Iodo-phenyl)-3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole

[0598] 5-(3-Iodo-phenyl)-3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole (725 mg, 97%, white solid) was obtained from 3-chloromethyl-5-(3-iodo-phenyl)-[1,2,4]oxadiazole (500 mg, 1.56 mmol), potassium carbonate (647 mg, 4.68 mmol), 4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazole-3-thiol (369 mg, 1.87 mmol) in acetonitrile (10 ml) at room temperature. Purification was performed by flash column chromatography on silica gel using 40% ethyl acetate in hexanes. ^{1}H NMR ($CDCl_3$), δ (ppm): 8.44 (d, 1H), 8.06 (d, 1H), 7.93 (d, 1H), 7.51 (m,

2H), 7.26 (t, 1H), 7.19 (m, 1H), 4.54 (s, 2H), 3.73 (s, 3H).

[0599] Example 78

[0600] 5-(3-Ethyl-phenyl)-3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole

[0601] 5-(3-Ethyl-phenyl)-3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole (28.1 mg, 27%, white solid) was obtained from 4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazole-3-thiol (59 mg, 0.30 mmol), 3-chloromethyl-5-(3-ethyl-phenyl)-[1,2,4]oxadiazole (60 mg, 0.27 mmol) and potassium carbonate (111 mg, 0.80 mmol) in acetonitrile (1 ml) at room temperature. Purification was performed by SPE (flash) chromatography using 50% ethyl acetate in hexane. ^{1}H NMR ($CDCl_3$), δ (ppm): 7.90 (t, 2H), 7.51 (m, 2H), 7.42 (t, 2H)7.18 (m, 1H), 4.52 (s, 2H), 3.72 (s, 3H), 2.70 (m, 2H), 1.26 (t, 3H)

[0602] Example 79

[0603] 2-[5-(2-Methyl-pyridin-4-yl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1*H*-benzoimidazole

[0604] 2-[5-(2-Methyl-pyridin-4-yl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1*H*-benzoimidazole (46.0 mg, 59%, white solid) was obtained from 2-mercaptobenzimidazole (41 mg, 0.27 mmol), 4-(3-chloromethyl-[1,2,4]oxadiazol-5-yl)-2-methyl-pyridine (50 mg, 0.24 mmol), and potassium carbonate (100 mg, 0.72 mmol) in DMF (1 ml) at room temperature. Purification was performed by SPE (flash) chromatography using 100% ethyl acetate and titurated with ether. ^{1}H NMR (DMSO-d_6), δ (ppm): 8.72 (d, 1H), 7.87 (s, 1H), 7.78 (d, 1H), 7.47 (t, 2H), 7.14 (m, 2H), 4.81 (s, 2H), 2.59 (s, 3H)

[0605] Example 80

[0606] 2-[5-(3-Iodo-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1*H*-benzoimidazole

[0607] 2-[5-(3-Iodo-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1*H*-benzoimidazole (36 mg, 51%, white solid) was obtained from 3-chloromethyl-5-(3-

iodo-phenyl)-[1,2,4]oxadiazole (50 mg, 0.16 mmol), potassium carbonate (65 mg, 0.47 mmol), 1*H*-benzoimidazole-2-thiol (23 mg, 0.16 mmol) in DMF (1 ml) at room temperature. Purification was performed by SPE (flash) chromatography using 50-100% ethyl acetate in hexanes followed by trituration with ethyl acetate. ^{1}H NMR (DMSO), δ (ppm): 12.73 (bs, 1H), 8.30 (s, 1H), 8.09 (d, 2H), 7.45 (m, 3H), 7.18 (m, 2H), 4.78 (s, 2H).

[0608] Example 81

[0609] 3-(4-Methyl-5-trifluoromethyl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole

[0610] 3-(4-Methyl-5-trifluoromethyl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole (54.3 mg, 80%, clear oil) was obtained from 3-chloromethyl-5-m-tolyl-[1,2,4]oxadiazole (40 mg, 0.19 mmol), potassium carbonate (79 mg, 0.58 mmol), 4-methyl-5-trifluromethyl-4*H*-[1,2,4]triazole-3-thiol (35.1 mg, 0.19 mmol) in acetonitrile (2 ml) at 60°C overnight. Purification was performed on silica gel using 50% ethyl acetate in hexanes. ^{1}H NMR ($CDCl_3$), δ (ppm): 7.87 (m, 2H), 7.41 (m, 2H), 4.59 (s, 2H), 3.69 (s, 3H), 2.43 (s, 3H).

[0611] Example 82

[0612] 2,6-Dichloro-4-[4-methyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4*H*-[1,2,4]triazol-3-yl]-pyridine

[0613] 2,6-Dichloro-4-[4-methyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4*H*- [1,2,4]triazol-3-yl]-pyridine (51.4 mg, 62%, off-white solid) was obtained from 3-chloromethyl-5-m-tolyl-[1,2,4]oxadiazole (40 mg, 0.19 mmol), potassium carbonate (79 mg, 0.58 mmol), 5-(2,6-dichloro-pyridin-4-yl)-4-methyl-4*H*-[1,2,4]triazole-3-thiol (50.1 mg, 0.19 mmol) in acetonitrile (2 ml) at 60°C overnight. Purification was performed on silica gel using 80% ethyl acetate in hexanes. ^{1}H NMR ($CDCl_3$), δ (ppm): 7.87 (m, 2H), 7.61 (s, 2H), 7.40 (m, 2H), 4.60 (s, 2H), 3.71 (s, 3H), 2.42 (s, 3H).

[0614] Example 83

[0615] 3-(4-Methyl-5-p-tolyl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole

[0616] 3-(4-Methyl-5-p-tolyl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole (57.8 mg, 81%, off-white solid) was obtained from 3-chloromethyl-5-m-tolyl-[1,2,4]oxadiazole (40 mg, 0.19 mmol), potassium carbonate (79 mg, 0.58 mmol), 4-methyl-5-p-tolyl-4*H*-[1,2,4]triazole-3-thiol (39.4 mg, 0.19 mmol) in acetonitrile (2 ml) at 60°C overnight. Purification was performed on silica gel using 80% ethyl acetate in hexanes. ^{1}H NMR ($CDCl_3$), δ (ppm): 7.88 (m, 2H), 7.53 (d, 2H), 7.39 (m, 2H), 7.30 (d, 2H), 4.55 (s, 2H), 3.59 (s, 3H), 2.42 (d, 6H).

[0617] Example 84

[0618] Dimethyl-{3-[3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]phenyl}-amine

[0619] Dimethyl-{3-[3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]phenyl}-amine (28.0 mg, 85%, white solid) was obtained from 4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazole-3-thiol (18 mg, 0.093 mmol), 3-(3-chloromethyl-[1,2,4]oxadiazol-5-yl)-phenyl]-dimethyl-amine (20 mg, 0.084 mmol), and potassium carbonate (35 mg, 0.25 mmol) in acetonitrile (1 ml) at room temperature. Purification was performed by SPE (flash) chromatography using 70% ethyl acetate in hexane. ^{1}H NMR ($CDCl_3$), δ (ppm): 7.49 (m, 2H), 7.36 (m, 3H), 7.17 (t, 1H), 6.91 (d, 1H), 4.51 (s, 2H), 3.72 (s, 3H), 3.00 (s, 6H)

[0620] Example 85

[0621] 5-(3-Chloro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole

[0622] 5-(3-Chloro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole (76.8 mg, 90%, white solid) was obtained from 4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazole-3-thiol (47 mg, 0.24 mmol), 3-chloromethyl-5-(3-chloro-phenyl)-[1,2,4]oxadiazole (50 mg, 0.22 mmol), and potassium carbonate (91 mg, 0.66 mmol) in acetonitrile (1 ml) at room temperature. Purification was performed by SPE (flash) chromatography using 70% ethyl acetate

in hexane. ^{1}H NMR ($CDCl_3$), δ (ppm): 8.09 (s, 1H), 7.98 (d, 1H), 7.49 (m, 4H), 7.18 (m, 1H), 4.55 (s, 2H), 3.73 (s, 3H)

[0623] Example 86

[0624] 3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-trifluoromethoxy-phenyl)[1,2,4]oxadiazole

[0625] 3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-trifluoromethoxy-phenyl)[1,2,4]oxadiazole (144.0 mg, 91%, white solid) was obtained from 4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazole-3-thiol (78 mg, 0.39 mmol), 3-chloromethyl-5-(3-trifluoromethoxy-phenyl)-[1,2,4]oxadiazole (100 mg, 0.36 mmol) and potassium carbonate (149 mg, 1.08 mmol) in acetonitrile (2 ml) at room temperature. Purification was performed by SPE (flash) chromatography using 55% ethyl acetate in hexane. ^{1}H NMR ($CDCl_3$), δ (ppm): 8.04 (d, 1H), 7.95 (s, 1H), 7.51 (m, 4H), 7.18 (m, 1H), 4.56 (s, 2H), 3.74 (s, 3H)

[0626] Example 87

[0627] 3-(5-Cyclohexyl-4-methyl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole

[0628] 3-(5-Cyclohexyl-4-methyl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole (10.5 mg, clear oil) was obtained from 3-chloromethyl-5-m-tolyl-[1,2,4]oxadiazole (50 mg, 0.24 mmol), potassium carbonate (165 mg, 1.20 mmol), 5-cyclohexyl-4-methyl-4*H*-[1,2,4]triazole-3-thiol (94.6 mg, 0.48 mmol) in acetonitrile (3 ml) at 60°C overnight. Purification was performed on silica gel using 2% ammonia (2 N methanol) in dichloromethane. ^{1}H NMR ($CDCl_3$), δ (ppm): 7.88 (m, 2H), 7.39 (m, 2H), 4.42 (s, 2H), 3.46 (s, 3H), 2.60 (m, 1H), 2.42 (d, 3H), 1.74 (m, 7H), 1.34 (m, 3H).

[0629] Example 88

[0630] 3-(5-tert-Butyl-4-methyl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole

[0631] 3-(5-tert-Butyl-4-methyl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-

[1,2,4]oxadiazole (56.8 mg, white solid) was obtained from 3-chloromethyl-5-m-tolyl-[1,2,4]oxadiazole (50 mg, 0.24 mmol), potassium carbonate (100 mg, 0.72 mmol), 5-tert-butyl-4-methyl-4*H*-[1,2,4]triazole-3-thiol (41 mg, 0.24 mmol) in acetonitrile (2 ml) at 60°C overnight. Purification was performed on silica gel using 80% ethyl acetate in hexanes. ^{1}H NMR ($CDCl_3$), δ (ppm): 7.89 (m, 2H), 7.40 (m, 2H), 4.46 (s, 2H), 3.63 (s, 3H), 2.43 (m, 3H), 1.45 (s, 9H).

[0632] Example 89

[0633] 5-(3-Bromo-phenyl)-3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole

[0634] 5-(3-Bromo-phenyl)-3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole (83.4 mg, 86%, white solid) was obtained from 4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazole-3-thiol (47 mg, 0.24 mmol), 5-(3-bromo-phenyl)-3-chloromethyl-[1,2,4]oxadiazole (60 mg, 0.22 mmol), and potassium carbonate (91 mg, 0.66 mmol) in acetonitrile (2 ml) at room temperature. Purification was performed by SPE (flash) chromatography using 60% ethyl acetate in hexane. ^{1}H NMR ($CDCl_3$), δ (ppm): 8.25 (t, 1H), 8.02 (d, 1H), 7.73 (d, 1H), 7.50 (m, 2H), 7.40 (t, 1H), 7.19 (m, 1H), 4.55 (s, 2H), 3.73 (s, 3H)

[0635] Example 90

[0636] 2-[5-(3-Bromo-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1*H*-benzoimidazole

[0637] 2-[5-(3-Bromo-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1*H*-benzoimidazole (71.1 mg, 84%, white solid) was obtained from 2-mercaptobenzimidazole (35 mg, 0.23 mmol), 5-(3-Bromo-phenyl)-3-chloromethyl-[1,2,4]oxadiazole (60 mg, 0.22 mmol) and potassium carbonate (91 mg, 0.66 mmol) in DMF (2 ml) at room temperature. Purification was performed by SPE (flash) chromatography using 35% ethyl acetate in hexane and titurated with ether. ^{1}H NMR (DMSO-d_6), δ (ppm): 12.78 (broad s, 1H), 8.18 (s, 1H), 8.07 (d, 1H), 7.93 (d, 1H), 7.59 (t, 1H), 7.46 (s, 2H), 7.14 (m, 2H), 4.77 (s, 2H)

[0638] Example 91

[0639] 5-(3-Methoxymethyl-phenyl)-3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-lsulfanylmethyl)-[1,2,4]oxadiazole

[0640] 5-(3-Methoxymethyl-phenyl)-3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-lsulfanylmethyl)-[1,2,4]oxadiazole (76 mg, 90%, white solid) was obtained from 3-chloromethyl-5-(3-methoxymethyl-phenyl)-[1,2,4]oxadiazole (50 mg, 0.21 mmol), potassium carbonate (87 mg, 0.63 mmol), 4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazole-3-thiol (50 mg, 0.25 mmol) in acetonitrile (2 ml) at room temperature. Purification was performed by SPE (flash) chromatography using 40-70% ethyl acetate in hexanes. ^{1}H NMR ($CDCl_3$), δ (ppm): 8.06 (s, 1H), 8.01 (d, 1H), 7.59 (d, 1H), 7.50 (m, 3H), 7.18 (t, 1H), 4.54 (s, 2H), 4.50 (s, 2H), 3.72 (s, 3H), 3.43 (s, 3H).

[0641] Example 92

[0642] 2-[5-(3-Methoxymethyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1*H*-benzoimidazole

[0643] 2-[5-(3-Methoxymethyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1*H*-benzoimidazole (62 mg, 84%, white solid) was obtained from 3-chloromethyl-5-(3-methoxymethyl-phenyl)-[1,2,4]oxadiazole (50 mg, 0.21 mmol), potassium carbonate (87 mg, 0.63 mmol), 1*H*-benzoimidazole-2-thiol (32 mg, 0.21 mmol) in DMF (2 ml) at room temperature. Purification was performed by SPE (flash) chromatography using 40-100% ethyl acetate in hexanes. ^{1}H NMR (DMSO), δ (ppm): 8.09 (d, 2H), 7.59 (m, 2H), 7.46 (bs, 2H), 7.14 (m, 2H), 4.77 (s, 2H), 4.51 (s, 2H), 3.35 (s, 3H).

[0644] Example 93

[0645] 4-[3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine

[0646] A solution of isonicotinoyl chloride (2.0 g, 11.2 mmol) in dichloromethane was treated with 2-chloro-*N*-hydroxy-acetamidine (1.58 g, 14.6 mmol), followed by addition of triethylamine (4.67 ml, 33.6 mmol) in a dropwise manner. After stirring at room temperature 1 h, extraction with ethyl acetate using water and brine washes afforded the oxy-acyl intermediate (used without further purification, 150 mg, 0.7

mmol). A solution of the crude product in acetonitrile (2 ml) and DMSO (2 ml) with K_2CO_3 (292 mg, 2.1 mmol) and 4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazole-3-thiol (140 mg, 0.7 mmol) was stirred at room temperature for 24 h followed by 1.5 h at 120°C (sealed tube). Standard aqueous work-up with ethyl acetate using water and brine washes followed by silica gel chromatography afforded the title compound (110 mg, 44%). ^{1}H NMR ($CDCl_3$), δ (ppm): 8.41 dd,2H), 7.92 dd,2H), 7.50 dd,1H), 7.47 dd,1H), 7.18 dd,1H), 4.58 (s,2H), 3.74 (s,3H); LC-MS $(M+H)^+$: 357.

[0647] Example 94 was prepared in an analogous method to the procedure given in Example 93.

[0648] <u>Example 94</u>

[0649] 4-[5-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-3-yl]-pyridine

[0650] 4-[5-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-3-yl]-pyridine (12 mg, 5%) was obtained from *N*-hydroxy-isonicotinamidine (200 mg, 1.4 mmol) with chloroacetyl chloride (0.11 ml, 1.4 mmol) and triethylamine (0.5 ml, 3.5 mmol); aqueous work-up gave intermediate (150 mg, 0.7 mmol); treated with K_2CO_3 (292 mg, 2.1 mmol), and 4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazole-3-thiol (140 mg, 0.7 mmol). Purification was performed by silica gel chromatography and recrystallization. ^{1}H NMR ($CDCl_3$), δ (ppm): 8.76 (dd,2H), 7.89 (dd,2H), 7.53 (dd,1H), 7.48 (dd,1H), 7.18 (dd,1H), 4.71 (s,2H), 3.73 (s,3H); LC-MS (M+H)+: 357.

[0651] <u>Example 95</u>

[0652] 2-{1-[5-(3-Methoxy-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-1-methyl-1*H*-imidazo[4,5-b]pyridine and 2-[5-(3-Methoxy-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1-methyl-1*H*-imidazo[4,5-b]pyridine

[0653] THF (3 ml) was added to a mixture of sodium hydride (60%, 8 mg, 0.2 mmol) and 2-[5-(3-methoxy-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1*H*-imidazo[4,5-b]pyridine (24.6 mg, 0.072 mmol) and the resulting mixture was stirred

at 0°C for about 15 min.. Methyl iodide (20 μL, 0.32 mmol) was added the resulting mixture was stirred at 0°C for 2h. The reaction was quenched by the addition of dichloromethane (10 ml) and water (2 ml). After vigorous stirring, the organic extracts (10 ml, plus 3x5 ml) were eluted through a Chem Elut Extraction Column (Varian, cat #1219-8002). Purification using SPE chromatography (5 g silica) using 25/25/50 to 50/25/25 ethyl acetate / dichloromethane / hexane yielded two products. The first product to elute was 2-{1-[5-(3-methoxy-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-1-methyl-1*H*-imidazo[4,5-b]pyridine (6 mg, 23%). ^{1}H NMR ($CDCl_3$), δ (ppm): 8.46 (d, 1H), 7.72 (d, 1H), 7.62 (d, 1H), 7.55 (d,1H), 7.42 (t,1H), 7.14 (m, 2H), 5.67 (q, 1H), 3.88 (s, 3H), 3.71 (s, 3H), 2.01 (d, 3H).

[0654] The second product to elute was 2-[5-(3-methoxy-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1-methyl-1H-imidazo[4,5-b]pyridine (12 mg, 47%). ^{1}H NMR ($CDCl_3$), δ (ppm): 8.44 (d, 1H), 7.69 (d, 1H), 7.60 (d, 1H), 7.55 (d, 1H), 7.41 (t, 1H), 7.13 (m, 1H), 4.90 (s, 2H), 3.87 (s, 3H), 3.70 (s, 3H).

[0655] Example 96-97 was prepared in an analogous method to the procedure given in Example 95.

[0656] Example 96

[0657] 3-[1-Methyl-1-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-5-m-tolyl-[1,2,4]oxadiazole

[0658] 3-[1-Methyl-1-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-5-m-tolyl-[1,2,4]oxadiazole (13 mg, 47%) was obtained from 3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole (25.5 mg, 0.069 mmol) with 60% sodium hydride (37 mg, 0.92 mmol) and methyl iodide (0.10 ml, 1.6 mmol) in THF (3 ml) at room temperature for 2 h. The product was extracted with ethyl acetate and purified by SPE 20-40% ethyl acetate in 1:1 dichloromethane : hexane. ^{1}H NMR ($CDCl_3$), δ (ppm): 7.83 (br s, 2H), 7.48 (d, 1H), 7.42 (d, 1H), 7.36 (m, 2H), 7.13 (m, 1H), 3.50 (s, 3H), 2.35 (s, 3H), 1.95 (s, 6H).

[0659] Example 97

[0660] 3-[1-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-5-m-tolyl-[1,2,4]oxadiazole

[0661] 3-[1-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-5-m-tolyl-[1,2,4]oxadiazole (6.1 mg, 17%) was obtained from 3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole (33.8 mg, 0.091 mmol) with 60% sodium hydride (17 mg, 0.42 mmol) and methyl iodide (20 µL, 0.32 mmol) in THF (2.5 ml) at room temperature for 1h. The product was extracted with dichloromethane and purified by SPE 25-40% ethyl acetate in 1:1 chloroform : hexane. ^{1}H NMR ($CDCl_3$), δ (ppm): 7.89 (br s, 2H), 7.50 (d, 1H), 7.46 (d, 1H), 7.38 (m, 2H), 7.16 (m, 1H) , 4.89 (q, 1H), 3.64 (s, 3H), 2.37 (s, 3H), 1.90 (d, 3H).

<u>[0662] Example 98</u>

[0663] 3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazole-3-sulfonylmethyl)-5-m-tolyl-[1,2,4]oxadiazole and 3-(4-Methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazole-3-sulfinylmethyl)-5-m-tolyl-[1,2,4]oxadiazole

[0664] Dichloromethane (2.5 ml) was added to a mixture of 3-chloro-benzenecarboperoxoic acid (57-85%, 49.5 mg, 0.16-0.25 mmol) and 3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole (45 mg, 0.12 mmol) and the resulting mixture was stirred at room temperature overnight. The reaction was quenched by the addition of dichloromethane (10 ml) and 1 M sodium hydroxide (3 ml). After vigorous stirring, the organic extracts (10 ml, plus 3x5 ml) were eluted through a Chem Elut Extraction Column (Varian, cat #1219-8002). Purification was performed by SPE chromatography (5 g silica) using 10-30% ethyl acetate in 1:1 dichloromethane : hexane yielded two products. The first product to elute was 3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazole-3-sulfonylmethyl)-5-m-tolyl-[1,2,4]oxadiazole (12.3 mg, 25%). ^{1}H NMR ($CDCl_3$), δ (ppm): 7.83 (br s, 2H), 7.63 (d, 1H), 7.56 (d, 1H), 7.36 (m, 2H), 7.24 (m, 1H), 5.12 (s, 2H), 3.94 (s, 3H), 2.36 (d, 3H).

[0665] The second product to elute was 3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazole-3-sulfinylmethyl)-5-m-tolyl-[1,2,4]oxadiazole (33.2 mg, 71%). ^{1}H NMR ($CDCl_3$), δ (ppm): 7.87 (br s, 2H), 7.59 (d, 1H), 7.54 (d, 1H), 7.38 (m, 2H), 7.22

(m, 1H) , 5.05 (d_{AB}, 1H) , 4.90 (d_{AB}, 1H), 4.03 (s, 3H), 2.39 (d, 3H).

[0666] Example 99

[0667] 5-(3-Furan-3-yl-phenyl)-3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole

[0668] To 5-(3-Iodo-phenyl)-3-(4-methyl-5-thiophen-2-yl-4*H*-[1,2,4]triazol-3-ylsulfanylmethyl) -[1,2,4]oxadiazole (50 mg, 0.10 mmol) in a vial was added 3-furan boronic acid (17 mg, 0.16 mmol), tetrakis(triphenylphosphine)palladium(0) (6 mg, 0.0052 mmol), ethylene glycol dimethyl ether (1 ml) and 2 M sodium carbonate (1 ml). The vial was then sealed and heated at 90°C for 1 h with vigorous stirring. The reaction was cooled, diluted with ethyl acetate, washed with water and saturated brine, filtered and concentrated. The residue was purified by flash column chromatography using 70% ethyl acetate in hexanes. Additional purification by trituration with a mixture of diethyl ether and hexanes and then filtration afforded the title compound as a beige solid 25 mg (57%). ^{1}H NMR ($CDCl_3$), δ (ppm): 8.18 (s, 1H), 7.98 (d, 1H), 7.79 (s, 1H), 7.71 (d, 1H), 7.51 (m, 4H), 7.17 (m, 1H), 6.74 (s, 1H), 4.55 (s, 2H), 3.73 (s, 3H).

[0669] Intermediates

[0670] Example 100

[0671] Pyrimidine-4-carboxylic acid.

[0672] 3-Methyl-pyrimidine (9.41 g, 100 mmol), potassium permanganate (26.9 g) and sodium carbonate (10.6 g) was refluxed in water (100 ml) for 72 h followed by filtration through celite. The filtrate was washed with several portions of DCM and EtOAc before acidification with conc. HCl. The formed precipitate was collected and washed with water to yield 1.37 g of the title compound as a white solid. 1H NMR (DMSO-d6) d (ppm): 13.94 (br. s, 1H), 9.37 (d, 1H), 9.07 (d, 1H), 8.01 (dd, 1H).

[0673] Example 101

[0674] 5-Chloro-thiophene-3-carboxylic acid.

[0675] Thiophene-3-carboxylic acid (17.51 g, 136.6 mmol) and 1-chloro-pyrrolidine-2,5-dione (23.7 g) was refluxed in acetic acid (200 ml) for 4 h under argon before pouring onto water (700 ml). Repeated extraction with several small portions of DCM, followed by back extraction from the combined organics with several small portions of 2 M aqueous sodium hydroxide, gave a combined alkaline aqueous solution that was washed with DCM before acidified with conc. HCl to precipitate the crude material. This precipitate was recrystallized from water to yield 14.98 g of the title compound as a grey solid contaminated with approximately 20 mol% of a dichlorinated byproduct as judged from MS and 1H-NMR. 1H NMR (DMSO-d6) d (ppm): 8.15 (d, 1H), 7.37 (d, 1H).

[0676] Example 102

[0677] 3-Methylsulfanyl-benzoic acid

[0678] Methyl iodide (0.972 mL) was added to a mixture of 3-mercapto-benzoic acid (601 mg, 3.9 mmol) and potassium carbonate (2.7 g, 19.5 mmol) in DMF (8 mL) in an ice-bath. After the reaction was warmed to room temperature and stirred for 1 hour, the reaction mixture was diluted with ethyl acetate, washed with water (3X), dried over anhydrous sodium sulfate, filtered, and concentrated to afford 3-methylsulfanyl-benzoic acid methyl ester (684 mg, 96%, yellow oil). ^{1}H NMR ($CDCl_3$), δ (ppm): 7.90 (s, 1H), 7.80 (d, 1H), 7.44 (d, 1H), 7.35 (t, 1H), 3.92 (s, 3H), 2.53 (s, 3H).

[0679] 3-Methylsulfanyl-benzoic acid methyl ester (684mg, 3.8 mmol) and 1N NaOH (5.6 mL, 5.6 mmol) in methanol (8 mL) and THF (8 mL) were heated at 70°C for 1 hour. The reaction mixture was concentrated and then the residue was diluted with water. After acidification with 1N HCl to pH ~ 2, the aqueous layer was extracted with ethyl acetate and then washed with water and saturated brine, dried over anhydrous sodium sulfate, filtered, and concentrated to afford 3-methylsulfanyl-benzoic acid (616 mg, 97%, white solid). ^{1}H NMR (DMSO), δ (ppm): 13.1 (bs, 1H), 7.76 (s, 1H), 7.70 (d, 1H), 7.51 (d, 1H), 7.44 (t, 1H), 2.52 (s, 3H).

[0680] Example 103

[0681] 3-Cyclopropyl-benzoic acid

[0682] 1.0 M Diethyl zinc in hexanes (27.3 ml, 27.3 mmol) was added to a solution of 2,4,6-trichlorophenol (5.4g, 27.3 mmol) in dichloromethane (100 ml) at –40°C. After stirring for 15 minutes, diiodo-methane (2.2 mL, 27.3 mmol) was added at –40°C and stirred for an additional 15 minutes. 1-Bromo-3-vinyl-benzene (2.5 g, 13.7 mmol) was then added to the reaction mixture, allowed to warm to room temperature, and left stirring overnight. The reaction mixture was diluted with dichloromethane, washed with 1N HCl (2X), saturated sodium bicarbonate (2X), saturated sodium sulfite, 1N sodium hydroxide, and saturated brine, dried over magnesium sulfate, filtered and concentrated. GC-MS revealed that the reaction mixture contained 1-Bromo-3-cyclopropyl-benzene and 1-bromo-3-vinyl-benzene.

[0683] To remove the bromo-3-vinyl-benzene, the crude mixture was reacted with potassium permanganate. A solution of potassium permanganate/water (1.5 g/20 mL) was added drop-wise to a solution of the crude mixture (~ 3.5 g) in THF (40 mL) at 0°C and then allowed to warm to room temperature. After 1 hour, the reaction was diluted with diethyl ether, washed with water and saturated brine, dried over anhydrous sodium sulfate filtered and concentrated. Purication by flash column chromatography eluted with 100 hexanes afforded 1-bromo-3-cyclopropyl-benzene (2.20g, 81%).

[0684] 1.6 M n-Butyllithium in hexanes (3.2 mL, 5.1 mmol) was added drop-wise to a solution of 1-bromo-3-cyclopropyl-benzene at –78°C and stirred for 1 hour. This reaction mixture was then transferred via canula to a 250 mL round bottom flask equipped with a stirrer bar approximately ¼ full of solid carbon dioxide and stirred and for 1 hour. The reaction mixture was concentrated and then the residue was diluted with water. The aqueous layer was washed with dichloromethane (3X), acidified with 1 N HCl to pH ~ 2, and extracted with ethyl acetate. The organic phase was washed with water and saturated brine, dried over anhydrous sodium sulfate, filtered and concentrated to afford 3-cyclopropyl-benzoic (356 mg, 43%, white solid). ^{1}H NMR (DMSO), δ (ppm): 12.90 (bs, 1H), 7.71 (d, 1H), 7.64 (s, 1H), 7.34 (m, 2H), 2.01 (m, 1H), 0.99 (m, 2H), 0.70 (m, 2H).

[0685] Example 104

[0686] 3-tert-Butoxycarbonylamino-benzoic acid

[0687] To a flask containing ethyl-3-aminobenzoate (1g, 6.05 mmol) added di-*tert*-butyl dicarbonate (3.16 g, 14.5 mmol), triethyl amine (500 mg, 4.94 mmol), and THF (10 mL) and allowed to stir at 60°C for two hours and then overnight at room temperature. The THF was removed *in vacuo,* and the crude ester was partitioned between ethyl acetate and water, washed with saturated brine, dried over anhydrous sodium sulfate and the solvent was removed *in vacuo*. The product was then purified by flash column chromatography using 15% ethyl acetate in hexane affording 2g of 3-tert-butoxycarbonylamino-benzoic aid ethyl ester (white slurry).

[0688] To the crude 3-tert-butoxycarbonylamino-benzoic acid ethyl ester (~2.0g, 0.00754 mmol) added THF (15 mL), and 0.5M LiOH (15 mL). The mixture was heated for two hours at 75°C and the THF was removed *in vacuo* after cooling. The precipitate was filtered from the remaining mixture and the filtrate was transferred to a separatory funnel. The aqueous layer was washed with dichloromethane (3x) and was acidified to pH ~5 using 1M HCl. The product was then extracted with ethyl acetate, washed with water, saturated brine, dried over anhydrous sodium sulfate, filtered and concentrated. 730mg of 3-tert-Butoxycarbonylamino-benzoic acid (white solid) was isolated. 1H NMR (DMSO-d_6) δ (ppm): 9.58 (s, 1H), 8.16 (s, 1H), 7.63 (d, 1H), 7.54 (d, 1H), 7.37 (t, 1H), 1.49 (s, 9H)

[0689] Example 105

[0690] 3-Acetyl-benzoic acid

[0691] 6M Sodium hydroxide (25 mL) was added to 3-acetylbenzonitrile (850 mg, 5.82 mmol) in methanol (25 mL) and then heated at 90°C overnight. After concentrating the reaction mixture, the aqueous layer was washed with dichloromethane (2x), then acidified pH ~ 3 with 12M HCl. The precipitate was extracted with ethyl acetate then washed with water and saturated brine, dried over anhydrous sodium sulfate filtered and concentrated to afford 3-ethylbenzoic acid as a colorless oil; 0.800g (92%). 1H NMR ($CDCl_3$) δ (ppm): 8.70 (s, 2H), 8.33 (d, 2H), 8.24 (d, 2H), 7.64 (t, 1H), 2.70 (s, 3H).

[0692] Example 106

[0693] 2-Methyl-isonicotinic acid hydrazide

[0694] Dichloromethane (10mL) was added to 2-methyl nicotinic acid hydrochloride salt (1.1g, 6.34 mmol) and oxalyl chloride (6.95mL, 13.9mmol) was added slowly under Argon while the flask was cooled in ice. Dimethylformamide (2 drops) was added and the reaction was allowed to stir overnight during which time it warmed to room temperature. The reaction was concentrated and THF (10mL) was added to the flask and it was placed in an ice bath. Methanol (5mL) was added and the reaction was allowed to stir for one hour. The reaction was concentrated and the residue was partitioned between $NaHCO_3$ (sat) and EtOAc. The product was extracted with EtOAc three times. The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and concentrated. Purification was performed by solid phase extraction tube (20% EtOAc/hexanes) gave the title compound as a clear oil. ^1H NMR $CDCl_3$ □(ppm): 8.51 (d, 1H), 7.57 (d, 1H), 7.51 (d, 1H), 3.82 (s, 3H), 2.50 (s, 3H).

[0695] 2-Methyl-isonicotinic acid methyl ester (316.5mg, 2.093mmol) was dissolved in MeOH (7mL) under Argon and hydrazine monohydrate 98% (1mL, 20.93mmol) was added. The reaction was allowed to stir under Argon at room temperature for eighteen hours. The reaction was concentrated to give the title compound (271.9mg, 86%) as a white solid. ^1H NMR $CDCl_3$ □(ppm): 8.59 (d, 1H), 7.50 (s, 1H), 7.38 (d, 1H), 3.09 (br. s, 3H), 2.60 (s, 3H).

[0696] Example 107

[0697] 5-Chloro-2-fluoro-benzoic acid hydrazide.

[0698] Step 1: 5-Chloro-2-fluoro-benzoic acid methyl ester: Methanol (20 ml) was added to a solution 5-chloro-2-fluoro-benzoyl chloride (1.2 g, 6.2 mmol) in dichloromethane (10 ml) in an ice-bath. The reaction mixture was warmed to room temperature, stirred for 3 h and then concentrated to afford 5-chloro-2-fluoro-benzoic acid methyl ester (1.17 g, 100%). 1H NMR ($CDCl_3$), δ (ppm): 7.93 (m, 1H), 7.48 (m, 1H), 7.12 (m, 1H), 3.96 (s, 3H). Step 2: 5-Chloro-2-fluoro-benzoic acid hydrazide: A

mixture of 5-chloro-2-fluoro-benzoic acid methyl ester (1.17 g, 6.2 mmol) and hydrazine monohydrate (0.451 ml, 9.3 mmol) in ethanol (20 ml) was stirred at room temperature overnight. The reaction mixture was concentrated and then the residue was triturated with diethyl ether to afford 5-chloro-2-fluoro-benzoic acid hydrazide (497 mg, 42%, white solid). 1H NMR (DMSO), δ (ppm): 9.66 (bs, 1H), 7.58 (m, 2H), 7.36 (m, 1H), 4.58 (bs, 2H).

[0699] Example 108 was prepared analogously to example 107.

[0700] Example 108

[0701] 3-Cyano-benzoic acid hydrazide

[0702] 3-cyano-benzoyl chloride (3g, 18.12 mmol) in dichlormethane (5 mL) and methanol (20 mL) was stirred at room temperature and overnight. The solvent was removed using a rotevaporator to afford a white solid (3.76g). ^{1}H NMR (DMSO) □ (ppm): 8.33 (m, 1H), 8.24 (m, 1H), 8.14 (m, 1H), 7.76 (m, 1H), 3.89 (d, 3H).

[0703] A mixture of 3-cyano-benzoic acid methyl ester (2 g, 12 mmol) and hydrazine monohydrate (0.60 mL, 12 mmol) in ethanol (10 mL) was stirred at room temperature overnight. The reaction mixture was concentrated and then the residue was triturated with diethyl ether to afford 3-cyano-benzoic acid hydrazide (1.02 g, 51%, pink solid). ^{1}H NMR (DMSO) □(ppm): 10.31 (s, 1H), 8.21 (m, 1H), 8.11 (m, 1H), 7.99 (m, 1H), 7.70 (m, 1H), 4.50 (s, 1H).

[0704] Example 109

[0705] 2-Chloro-isonicotinic acid hydrazide

[0706] HOBt (823 mg, 6.09 mmol), and EDCI (1.2 g, 6.09 mmol) were added to a suspension of 2-chloro-isonicotinic acid (800 mg, 5.08 mmol) in acetonitrile (10.3 ml) at room temperature. After two h a solution of hydrazine monohydrate (0.493 ml, 10.2 mmol) in acetonitrile (5.0 ml) was added drop-wise at 0°C. After 30 min, the solvent was removed using a roto-evaporator and the residue was diluted with ethyl acetate, quenched with water, dried over sodium sulfate, filtered and concentrated to afford 2-chloro-isonicotinic acid hydrazide (493 mg, 57%, yellow solid). 1H NMR (DMSO) d (ppm): 10.21 (bs, 1H), 8.55 (d, 1H), 7.82 (s, 1H), 7.75 (d, 1H), 4.69 (bs, 2H).

[0707] The following compounds were prepared analogously to example 109:

Example No.	1) Name
110	2-Fluoro-5-methyl-benzoic acid hydrazide
111	Pyrimidine-4-carboxylic acid hydrazide

[0708] The following compounds were prepared analogously to Example 6:

Example No.	Name
112	3-Fluoro-N-hydroxy-benzamidine
113	N-Hydroxy-thiophene-3-carboxamidine
114	2-Chloro-N-hydroxy-propionamidine
115	3,N-Dihydroxy-benzamidine
116	N-Hydroxy-2-methyl-benzamidine
117	N-Hydroxy-2-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-acetamidine
118	3-Chloro-N-hydroxy-benzamidine
119	N-Hydroxy-2-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-acetamidine
120	2,5-Difluoro-N-hydroxy-benzamidine

[0709] The following compounds were prepared analogously to Example 31:

Example No.	Name
121	4-Methyl-5-pyridin-3-yl-4H-[1,2,4]triazole-3-thiol
122	4-Butyl-5-thiophen-2-yl-4H-[1,2,4]triazole-3-thiol
123	4-(3-Methoxy-propyl)-5-thiophen-2-yl-4H-[1,2,4]triazole-3-thiol
124	4-Benzyl-5-thiophen-2-yl-4H-[1,2,4]triazole-3-thiol
125	4-Furan-2-ylmethyl-5-thiophen-2-yl-4H-[1,2,4]triazole-3-thiol
126	5-Thiophen-2-yl-4-thiophen-2-ylmethyl-4H-[1,2,4]triazole-3-thiol
127	4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazole-3-thiol

128	4-Furan-2-ylmethyl-5-pyridin-4-yl-4H-[1,2,4]triazole-3-thiol
129	4-Ethyl-5-pyridin-4-yl-4H-[1,2,4]triazole-3-thiol
130	4-Ethyl-5-pyridin-3-yl-4H-[1,2,4]triazole-3-thiol
131	4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazole-3-thiol
132	4-Furan-2-ylmethyl-5-pyridin-3-yl-4H-[1,2,4]triazole-3-thiol
133	4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazole-3-thiol
134	4-Ethyl-5-(3-fluoro-phenyl)-4H-[1,2,4]triazole-3-thiol
135	4-Ethyl-5-(4-fluoro-phenyl)-4H-[1,2,4]triazole-3-thiol
136	5-(2-Fluoro-5-methyl-phenyl)-4-furan-2-ylmethyl-4H-[1,2,4]triazole-3-thiol
137	4-Ethyl-5-(3-methyl-thiophen-2-yl)-4H-[1,2,4]triazole-3-thiol
138	4-Ethyl-5-(5-methyl-thiophen-2-yl)-4H-[1,2,4]triazole-3-thiol
139	5-(2-Chloro-6-methyl-pyridin-4-yl)-4-ethyl-4H-[1,2,4]triazole-3-thiol
140	5-(5-Bromo-furan-2-yl)-4-ethyl-4H-[1,2,4]triazole-3-thiol
141	4-Ethyl-5-(3-methoxy-thiophen-2-yl)-4H-[1,2,4]triazole-3-thiol
142	4-Ethyl-5-(tetrahydro-furan-2-yl)-2,4-dihydro-[1,2,4]triazole-3-thione
143	4-Ethyl-5-thioxo-4,5-dihydro-1H-[1,2,4]triazole-3-carboxylic acid methyl ester

[0710] The following compounds were prepared analogously to Example 36:

Example No.	Name
144	5-(2-Chloro-pyridin-4-yl)-4-ethyl-4H-[1,2,4]triazole-3-thiol
145	5-(2-Chloro-6-methoxy-pyridin-4-yl)-4-ethyl-4H-[1,2,4]triazole-3-thiol
146	4-Ethyl-5-(3-methyl-3H-imidazol-4-yl)-4H-[1,2,4]triazole-3-thiol
147	4-Propyl-5-pyridin-4-yl-4H-[1,2,4]triazole-3-thiol
148	4-Ethyl-5-(1-methyl-1H-imidazol-2-yl)-4H-[1,2,4]triazole-3-thiol
149	4-Ethyl-5-(1-methyl-1H-imidazol-4-yl)-4H-[1,2,4]triazole-3-thiol
150	3-(5-Mercapto-4-methyl-4H-[1,2,4]triazol-3-yl)-benzonitrile
151	5-(3-Chloro-phenyl)-4-methyl-4H-[1,2,4]triazole-3-thiol
152	5-(4-Chloro-phenyl)-4-methyl-4H-[1,2,4]triazole-3-thiol
153	5-(2-fluoro-phenyl)-4-methyl-4H-[1,2,4]triazole-3-thiol

154	5-(3-fluoro-phenyl)-4-methyl-4H-[1,2,4]triazole-3-thiol
155	5-(4-fluoro-phenyl)-4-methyl-4H-[1,2,4]triazole-3-thiol
156	5-Benzo[b]thiophen-2-yl-4-methyl-4H-[1,2,4]triazole-3-thiol
157	5-(3-methoxy-phenyl)-4-methyl-4H-[1,2,4]triazole-3-thiol
158	5-(4-methoxy-phenyl)-4-methyl-4H-[1,2,4]triazole-3-thiol
159	4-Ethyl-5-(4-methoxy-phenyl)-4H-[1,2,4]triazole-3-thiol
160	5-(3,5-Difluoro-phenyl)-4-ethyl-4H-[1,2,4]triazole-3-thiol
161	5-(2,6-Difluoro-phenyl)-4-ethyl-4H-[1,2,4]triazole-3-thiol
162	5-(4-Butoxy-phenyl)-4-ethyl-4H-[1,2,4]triazole-3-thiol
163	5-Benzo[1,3]dioxol-5-yl-4-ethyl-4H-[1,2,4]triazole-3-thiol
164	4-Ethyl-5-pyrimidin-5-yl-2,4-dihydro-[1,2,4]triazole-3-thione
165	4-Ethyl-5-furan-3-yl-2,4-dihydro-[1,2,4]triazole-3-thione
166	4-(Tetrahydrofuran-2-ylmethyl)-5-thiophene-2-yl-2,4-dihydro-[1,2,4]triazole-3-thione
167	5-Cyclopentyl-4-ethyl-2,4-dihydro-[1,2,4]triazole-3-thione
168	4-Ethyl-5-[2-(4-methoxy-phenyl)-ethyl]-2,4-dihydro-[1,2,4]triazole-3-thione

[0711] Example 169

[0712] 5-(3,5-Dichloro-phenyl)-4-ethyl-4H-[1,2,4]triazole-3-thiol

[0713] 3,5-Dichloro-benzoic acid (382 mg, 2 mmol) was mixed with triethylamine (606 mg, 3 mmol) in THF (6 ml) at 10 °C. Then isobutyl chloroformate (300 mg, 2.2 mmol) was added dropwise and stirred for 45 min. To the reaction mixture, 4-methyl-3-thiosemicarbazide (238.4 mg, 2 mmol) was added. After being stirred at room temperature for 10 min, the reaction mixture was heated to 70 °C overnight. Standard work-up. The product was purified by column chromatography with 25~30 % ethyl acetate in hexanes to give 46.4 mg (8.5 %) of 5-(3,5-dichloro-phenyl)-4-ethyl-4H-[1,2,4]triazole-3-thiol.

[0714] The following compounds were prepared analogously to Example 169:

Example No.	Name
170	5-(3-Methylphenyl)-4-ethyl-4H-[1,2,4]triazole-3-thiol
171	5-(4-Methylphenyl)-4-ethyl-4H-[1,2,4]triazole-3-thiol
172	4-Ethyl- 5-(3-nitrophenyl)-4H-[1,2,4]triazole-3-thiol
173	5-(2,5-Difluorophenyl)-4-ethyl-4H-[1,2,4]triazole-3-thiol
174	5-(3-Chlorophenyl)-4-ethyl-4H-[1,2,4]triazole-3-thiol
175	5-(4-Chlorophenyl)-4-ethyl-4H-[1,2,4]triazole-3-thiol

[0715] Example 176

[0716] 4-Ethyl-5-methoxymethyl-2,4-dihydro-[1,2,4]triazole-3-thione

[0717] Step 1: N-Ethyl-2-(methoxyacetyl)hydrazinecarbothioamide: Methoxyacetic acid (360 mg, 3.99 mmol), 4-ethyl-3- thiosemicarbazide (581 mg, 4.87 mmol), diisopropylcarbodiimide (615 mg, 4.87 mmol) and hydroxybenzotriazole (69.6 mg, 0.51 mmol) were mixed in dimethylformamide (10 ml) and stirred under argon at ambient temperatures for 19 h. After evaporation to dryness the crude was used directly in the next step. MS (ESI) m/z 192 (M+1). Step 2: 4-Ethyl-5-methoxymethyl-2,4-dihydro-[1,2,4]triazole-3-thione: N-Ethyl-2-(methoxyacetyl)hydrazinecarbothioamide (760 mg crude, 4 mmol) and sodium bicarbonate (560 mg, 6.6 mmol) were suspended in water (15 ml) and refluxed for 5 h. After cooling and filtration the filtrate was acidified with concentrated hydrochloric acid, followed by extraction with ethyl acetate. After evaporation to dryness the crude was recrystallized in ethyl acetate/heptane. Filtration and recrystallization of the mother liquor gave a combined yield of 325 mg (47%) of the title compound. 1H NMR ($CDCl_3$), δ (ppm): 4.47 (s, 2H), 4.13 (q, 2H), 3.37 (s, 3H), 1.38 (t, 3H).

[0718] The following compounds were prepared analogously to Example 176:

Example No.	Name
177	4-Methyl-5-pyridin-4-yl-2,4-dihydro-[1,2,4]triazole-3-thione
178	4-Allyl-5-furan-2-yl-2,4-dihydro-[1,2,4]triazole-3-thione
179	4-Ethyl-5-(4-methoxy-phenoxymethyl)-2,4-dihydro-[1,2,4]triazole-3-thione

180	4-Ethyl-5-phenoxymethyl-2,4-dihydro-[1,2,4]triazole-3-thione
181	4-Ethyl-5-hydroxymethyl-2,4-dihydro-[1,2,4]triazole-3-thione
182	4-Ethyl-5-(2-methoxy-ethyl)-2,4-dihydro-[1,2,4]triazole-3-thione
183	4-Ethyl-5-methylsulfanylmethyl-2,4-dihydro-[1,2,4]triazole-3-thione
184	5-Ethoxymethyl-4-ethyl-2,4-dihydro-[1,2,4]triazole-3-thione
185	5-Furan-3-yl-4-methyl-2,4-dihydro-[1,2,4]triazole-3-thione
186	4-Methyl-5-pyrimidin-4-yl-2,4-dihydro-[1,2,4]triazole-3-thione
187	4-Ethyl-5-pyridazin-4-yl-2,4-dihydro-[1,2,4]triazole-3-thione
188	4-Ethyl-5-pyridin-4-ylmethyl-2,4-dihydro-[1,2,4]triazole-3-thione
189	4-Ethyl-5-(6-hydroxy-pyridin-3-yl)-2,4-dihydro-[1,2,4]triazole-3-thione
190	4-Ethyl-5-(4-hydroxy-phenyl)-2,4-dihydro-[1,2,4]triazole-3-thione
191	4-Ethyl-5-p-tolyloxymethyl-2,4-dihydro-[1,2,4]triazole-3-thione
192	4-Ethyl-5-(6-methoxy-pyridin-3-yl)-2,4-dihydro-[1,2,4]triazole-3-thione
193	4-Ethyl-5-(2-methoxy-pyridin-4-yl)-2,4-dihydro-[1,2,4]triazole-3-thione
194	4-Ethyl-5-pyrimidin-2-yl-2,4-dihydro-[1,2,4]triazole-3-thione
195	4-Ethyl-5-(5-methoxy-pyrimidin-2-yl)-2,4-dihydro-[1,2,4]triazole-3-thione

[0719] Example 196

[0720] 4-Furan-2-ylmethyl-4H-[1,2,4]triazole-3-thiol

[0721] A solution of formic acid hydrazide (439 mg, 7.809 mmol) in pyridine (20 ml) was added to a solution of 2-isothiocyanatomethyl-furan (1 g, 7.185 mmol) in pyridine (20ml). Reaction took place at room temperature overnight, and ethanol (20 ml) was added directly to the reaction and placed in 80C bath overnight. Solvent was evaporated and the title compound (1.09 g, 83%) was obtained from purification by SPE chromatography on silica gel with 500 ml 20%, 250 ml 25%, 250 ml 30%, 250 ml 35%, 250 ml 40%, and 250 ml 50% ethyl acetate in hexanes. 1H NMR (CD3OD), δ (ppm): 14.0 (bs, 1H), 8.19 (s, 1H), 7.52 (q, 1H), 6.52 (m, 1H), 6.42 (m, 1H), 4.90 (s, 2H).

[0722] The following compounds were prepared analogously to Example 196:

Example No.	Name
197	4-Cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazole-3-thiol
198	4-Cyclopropylmethyl-5-pyridin-4-yl-4H-[1,2,4]triazole-3-thiol

[0723] Example 199

[0724] 4-Cyclopropyl-5-thiophen-2-yl-2,4-dihydro-[1,2,4]triazole-3-thione

[0725] To a slurry of thiophene-2-carboxylic acid hydrazide (866 mg, 6.09 mmol) in iPrOH (25 ml) was added isothiocyanato-cyclopropane (602 mg, 6.08 mmol). The mixture was stirred at 70 °C for 72 h and then cooled to room temperature. The white precipitate was filtered off and suspended in a MeOH:H_2O (9:1, 40 ml) together with aq. NaOH (2%, 5 ml). The reaction mixture was stirred at 70 °C overnight and then cooled to room temperature. The pH was adjusted to around 4 with aq. HCl (1N). The formed white precipitate was filtered off, washed with water and dried under vacuum (829 mg, 61%). 1H NMR (CD3OD), δ (ppm): 7.67 (dd, 1H), 7.63 (dd, 1H), 7.17 (dd, 1H), 3.15 (m, 1H), 1.14 (m, 2H), 0.86 (m, 2H).

[0726] The following compounds were prepared analogously to Example 199:

Example No.	Name
200	5-Furan-2-yl-4-(2-methoxy-ethyl)-2,4-dihydro-[1,2,4]triazole-3-thione
201	4-Cyclopropyl-5-furan-2-yl-2,4-dihydro-[1,2,4]triazole-3-thione
202	(3-Thiophen-2-yl-5-thioxo-1,5-dihydro-[1,2,4]triazol-4-yl)-acetic acid methyl ester
203	4-Cyclopropylmethyl-5-thiophene-2-yl-2,4-dihydro-[1,2,4]triazole-3-thione
204	4-(2-Methoxy-ethyl)-5-thiophen-2-yl-2,4-dihydro-[1,2,4]triazole-3-thione
205	Thiophen-2-yl-4-(2,2,2-trifluoroethyl)-2,4-dihydro-[1,2,4]triazole-3-thione
206	4-Cyclopropyl-5-pyrimidin-4-yl-2,4-dihydro-[1,2,4]triazole-3-thione
207	4-Cyclopropyl-5-pyridin-3-yl-2,4-dihydro-[1,2,4]triazole-3-thione

[0727] Example 208

[0728] 4-Ethyl-5-trifluoromethyl-4H-[1,2,4]triazole-3-thiol

[0729] To a solution of 4-ethyl-3-thiosemicarbazide(2.38 g, 20 mmol) and triethylamine (6.06 g, 60 mmol) in THF (30 ml), trifluoroacetic anhydride (5.04 g, 24 mmol) was added. The reaction mixture was stirred at room temperature for an h and and heated at 60 °C overnight. Standard work-up, the product was triturated with hexanes to give 564g of as 4-ethyl-5-trifluoromethyl-4H-[1,2,4]triazole-3-thiol pale-brown solid. 1H-NMR(CDCl3) d(ppm): 12.64 (w, 1H), 4.22 (q, 2H) and 1.44 (t, 3H).

[0730] Example 209

[0731] 4-Ethyl-3-methanesulfonyl-5-thiophen-2-yl-4H-[1,2,4]triazole

[0732] The title compound was synthesized according to the method described in Åkerblom et al. J. Med. Chem. 16, 312 (1973). 4-Ethyl-3-methylsulfanyl-5-thiophen-2-yl-4H-[1,2,4]triazole (1.14 g, 5.06 mmol) was dissolved in glacial acetic acid (20 ml) followed by the addition of 30% hydrogen peroxide (5 ml). After stirring at ambient temperatures for 16 h additional 30% hydrogen peroxide (5 ml) was added. The mixture was stirred for 3 h at ambient temperature, then heated to 100 °C for 2.5 h. After cooling in an ice/water bath the reaction was neutralized with sodium hydroxide and extracted twice with dichloromethane. The organic layers were combined, evaporated to dryness and dried in vacuo yielding the title compound (0.78 g, 60%). 1H NMR (CDCl3), δ (ppm): 7.60 (d, 1H), 7.56 (d, 1H), 7.22 (m, 1H), 4.51 (q, 2H), 3.58 (s, 3H), 1.55 (t, 3H).

[0733] The following compound was prepared analogously to Example 209:

Example No.	Name
210	4-(5-Methanesulfonyl-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine

[0734] Example 211

[0735] 4-(2-Hydroxy-ethyl)-5-thiophen-2-yl-2,4-dihydro-[1,2,4]triazole-3-thione

[0736] To a slurry of LAH (38.1 mg, 1.00 mmol) in anhydrous THF (8 ml) was drop wise added (3-thiophen-2-yl-5-thioxo-1,5-dihydro-[1,2,4]triazol-4-yl)-acetic acid (101 mg, 0.42 mmol) in anhydrous THF (4 ml). The mixture was reacted for 2 h and then quenched with saturated aq. Na_2SO_4 (10 ml). THF was removed under reduced

pressure and the residue was made acidic with aq. HCl (3N) and partitioned between EtOAc and water. The aqueous layer was extracted with EtOAc (3 x 20 ml). The combined organic layers were washed with brine (15 ml), dried ($MgSO_4$) and concentrated under reduced pressure. The crude product was used without purification in the next step.1H NMR (DMSO-d6), δ (ppm): 13.94 (s, 1H), 7.86 (d, 1H); 7.81 (d, 1H), 7.24 (dd, 1H), 5.09 (t, 1H), 4.16 (t, 2H), 3.76 (app. q, 2H).

[0737] Example 212

[0738] 4-(4,5-Dimethyl-4H-[1,2,4]triazol-3-yl)-pyridine

[0739] 860 μl (10 mmol) oxalyl chloride was slowly added to a solution of 731 mg (10 mmol) N-methyl-acetamide and 2.33 ml (20 mmol) 2,6-lutidine in 20 ml CH_2Cl_2 at 0°C. After 15 min 1.37 g (10 mmol) isonicotinic acid hydrazide was added in one portion. The resulting mixture was stirred at room temperature for 1h and the neutralized with $NaHCO_3$(sat). The phases were separated and the water phase was extracted with CH_2Cl_2. The combined organic phases were dried and concentrated. The residue was dissolve in 20 ml acetic acid and heated at 120°C for 2h. After cooling the solvent was removed. Flashchromatography (CH2Cl2/MeOH 10:1) afforded 765 mg (44%) of a grey/white solid. 1H NMR (CDCl3), d (ppm): 2.52 (s, 3 H) 3.66 (s, 3 H) 7.58 (d, 2 H) 8.76 (d, 2 H).

[0740] Example 213

[0741] Methyl-(4-methyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-yl)-amine

[0742] A mixture of 1000 mg (4.35 mmol) N-amino-N',N''-dimethyl-guanidine hydriodide (Henry; Smith; J.Amer.Chem.Soc.; 73; 1951; 1858) and 774 mg (4.35 mmol) isonicotinoyl chloride hydrochloride in 3ml of pyridine was heated with microwaves for 5 min at 160°C. K_2CO_3(sat) was added and the mixture was extracted 4 times with $CHCl_3$. The organic phase was dried and concentrated. Recrystallization from ethanol, water and EtOAc gave 216 mg (26%) of a yellow white solid. 1H NMR (DMSO), d (ppm): 2.85 (d, 3 H) 3.45 (s, 3 H) 6.25 (d, 1 H) 7.65 (m, 2 H) 8.67 (m, 2 H).

[0743] Example 214

[0744] 3-Pyridin-4-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrimidine

[0745] A solution of 750 mg (3.1 mmol) (1,4,5,6-tetrahydro-pyrimidin-2-yl)-hydrazine hydroiodide (ref. Krezel, Izabella; Pharmazie; EN; 49; 1; 1994; 27-31) and 552 mg (3.1 mmol) isonicotinoyl chloride hydrochloride in 3 ml pyridine was heated at 120 °C over night. The reaction mixture was cooled and diluted with K_2CO_3(sat) and extracted with 3x10 ml chloroform. The combined organic extracts were dried and concentrated. Flashchromatography (CH_2Cl_2/MeOH 10:1) afforded 83 mg (18%) of a white solid. 1H NMR ($CDCl_3$), d (ppm): 1.91 (m, 2 H) 3.24 (m, 2 H) 4.13 (m, 2 H) 7.67 (m, 2 H) 8.65 (m, 2 H).

[0746] The following compound was prepared analogously to Example 214:

Example No.	Name
215	3-Furan-2-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrimidine

[0747] Example 216

[0748] 4-Ethyl-5-(6-methoxy-pyridazin-3-yl)-2,4-dihydro-[1,2,4]triazole-3-thione

[0749] Step 1: 6-Chloro-pyridazine-3-carboxylic acid: Potassium dichromate (3.3 g, 11.2 mmol) was added in portions to a solution of 3-Chloro-6-methyl-pyridazine (1.2 g, 9.3 mmol) in H_2SO_4 (10 ml). After addition the mixture is stirred at 50 °C on. The reaction was pored on ice and the mixture was extracted three times with diethyl ether. The combined organic phases were dried and concentrated to give the title compound (840 mg, 57%). LC-MS (M++1): 159 and 161 (3:1). Step 2: 6-Chloro-pyridazine-3-carboxylic acid methyl ester: A solution of 6-chloro-pyridazine-3-carboxylic acid (700 mg, 4.53mmol) in thionyl chloride (15 ml) was refluxed for 3 h. The reaction was cooled to ambient temperature and evaporated to dryness. Sodium methoxide (244 mg, 4.53 mmol) in MeOH (20 ml) was added to the residue and the solution was stirred on at room temperature (rt). H_2O was added and the mixture was extracted three times with DCM. The combined organic phases were dried and concentrated. Flashchromatography (SiO_2, Heptane/EtOAc 1:1) afforded 560 mg

(72%) of the title compound.1H NMR ($CDCl_3$), δ (ppm): 4.09 (s, 3 H), 7.69 (d, 1 H), 8.18 (d, 1 H).LC-MS (M++1): 173 and 175 (3:1). Step 3: 6-Methoxy-pyridazine-3-carboxylic acid methyl ester: A solution of 6-chloro-pyridazine-3-carboxylic acid methyl ester in NaOMe in MeOH (1M, 10ml) was refluxed on. H_2O was added and the mixture was extracted three times with DCM to give organic phase I. The combined organic phases I were dried and concentrated to give the title compound (40 mg, 10%). The water phase was acidified with concentrated hydrochloric acid and extracted three times with DCM to give organic phase II. The combined organic phases II were dried and concentrated to give 6-methoxy-pyridazine-3-carboxylic acid (LC-MS (M++1): 155) (230 mg, 65%). A solution of 6-methoxy-pyridazine-3-carboxylic acid in thionyl chloride (6 ml) was refluxed for 3 h. The reaction was cooled to ambient temperature and evaporated to dryness. MeOH (10 ml) was added to the residue and the solution was stirred on at rt. Saturated $NaHCO_3$ (aq) was added and the mixture was extracted three times with DCM. The combined organic phases were dried and concentrated to give the title compound (253 mg, 100%).LC-MS (M++1): 169. Step 4: 4-Ethyl-5-(6-methoxy-pyridazin-3-yl)-2,4-dihydro-[1,2,4]triazole-3-thione: NaOMe (86 mg, 1.6 mmol) was added to a solution of 6-methoxy-pyridazine-3-carboxylic acid methyl ester (210 mg, 1.25 mmol) and 4-ethyl-3-thiosemicarbazide (190 mg, 1.6 mmol) in MeOH (6 ml) and the mixture was heated to 70°C at 72 h. The reaction was cooled to ambient temperature and evaporated to dryness. H_2O (10 ml) was added to the residue and the mixture was acidified with concentrated hydrochloric acid and the title compound 35 mg (12%) was collected by filtration. LC-MS (M++1): 238.

[0750] Example 217

[0751] 4-Ethyl-5-(5-methoxy-pyridin-2-yl)-2,4-dihydro-[1,2,4]triazole-3-thione

[0752] Step 1: 5-Methoxy-pyridine-2-carboxylic acid methyl ester: 5-Methoxy-2-methyl-pyridine (700 mg, 5.69 mmol) was dissolved in H_2O (20 ml) and heated to 80 °C. $KMnO_4$ (4 g, 25.3 mmol) was added in portion to the solution over 1 h. After stirring at 80 °C for 5 h the mixture was filtrated and the filtrate was washed with H_2O (60 °C). The combined water phase was concentrated. DMF (20 ml), K_2CO_3 (785 mg,

5.7 mmol) followed by MeI (540 ml, 8.6 mmol) was added to the remaining residue and the mixture was heated to 80 °C on. The reaction was cooled to ambient temperature and H_2O was added and the mixture was extracted three times with toluene. The combined organic phases were dried and concentrated. Flashchromatography (SiO_2, Heptane/EtOAc 1:1) afforded 210 mg (22%) of the title compound.1H NMR ($CDCl_3$):d ppm 3.93 (s, 3 H) 4.00 (s, 3 H) 7.23 (m, 1 H) 8.13 (d, 1 H) 8.40 (d, 1 H). Step 2: 4-Ethyl-5-(5-methoxy-pyridin-2-yl)-2,4-dihydro-[1,2,4]triazole-3-thione: NaOMe (4 ml, 4.0 mmol, 1M) was added to a solution of 5-Methoxy-pyridine-2-carboxylic acid methyl ester (200 mg, 1.2 mmol), 4-ethyl-3-thiosemicarbazide (145 mg, 1.2 mmol) in MeOH (10 ml) and the mixture was heated to 70°C on. The reaction was cooled to ambient temperature and evaporated to dryness. H_2O (10 ml) was added to the residue and the mixture was acidified with concentrated hydrochloric acid and the title compound 50 mg (18%) was collected by filtration. LC-MS (M++1): 237.

[0753] The following compounds were prepared analogously to example 10:

Example No.	Name
218	5-Chloromethyl-3-phenyl-[1,2,4]oxadiazole
219	5-Chloromethyl-3-(3-fluoro-phenyl)-[1,2,4]oxadiazole
220	5-Chloromethyl-3-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazole
221	5-Chloromethyl-3-thiophen-2-yl-[1,2,4]oxadiazole
222	5-Chloromethyl-3-thiophen-3-yl-[1,2,4]oxadiazole
223	3-(5-Chloromethyl-[1,2,4]oxadiazol-3-yl)-phenol
224	5-Chloromethyl-3-o-tolyl-[1,2,4]oxadiazole
225	5-Chloromethyl-3-(3-chloro-phenyl)-[1,2,4]oxadiazole
226	5-Chloromethyl-3-(2,5-difluoro-phenyl)-[1,2,4]oxadiazole

[0754] The following compounds were prepared analogously to example 16:

Example No.	Name

227	3-(3-Chloromethyl-[1,2,4]oxadiazol-5-yl)-benzonitrile
228	2-Chloro-4-(3-chloromethyl-[1,2,4]oxadiazol-5-yl)-pyridine
229	3-Chloromethyl-5-(2,5-dimethyl-phenyl)-[1,2,4]oxadiazole
230	3-Chloromethyl-5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazole
231	3-Chloromethyl-5-(2,5-dichloro-phenyl)-[1,2,4]oxadiazole
232	3-Chloromethyl-5-(2-fluoro-5-bromo-phenyl)-[1,2,4]oxadiazole
233	3-Chloromethyl-5-(3-methyl-phenyl)-[1,2,4]oxadiazole
234	3-Chloromethyl-5-(2,5-difluoro-phenyl)-[1,2,4]oxadiazole
235	3-Chloromethyl-5-(3-methylsulfanyl-phenyl)-[1,2,4]oxadiazole
236	3-Chloromethyl-5-(3-cyclopropyl-phenyl)-[1,2,4]oxadiazole
237	3-(3-Chloromethyl-[1,2,4]oxadiazol-5-yl)-phenyl]-carbamic acid tert-butyl ester
238	1-[3-(3-Chloromethyl-[1,2,4]oxadiazol-5-yl)-phenyl]-ethanone
239	5-(5-Chloro-2-fluoro-phenyl)-3-chloromethyl-[1,2,4]oxadiazole
240	2-(3-Chloromethyl-[1,2,4]oxadiazol-5-yl)-4-methyl-phenol

[0755] Example 241

[0756] 3-Chloromethyl-5-(2-chloro-5-methyl-phenyl)-[1,2,4]oxadiazole

[0757] 2-Chloro-5-methyl-benzoic acid (1g, 5.8 mmol) was treated with 5 ml thionyl chloride at reflux for two h. Excess thionyl chloride was removed under reduced pressure. The residue was added to a suspension of 2-chloro-N-hydroxy-acetamidine (638 mg, 5.8 mmol) in dichloromethane (10 ml) at room temperature. After stirring for 30 min, triethylamine (2.04 ml, 14.6 mmol) was added and stirred for an additional h. The reaction mixture was diluted with ethyl acetate, washed with water and brine, dried over anhydrous sodium sulfate, filtered and concentrated. Flash column chromatography using 10 – 20% ethyl acetate in hexanes afforded 460 mg of the acyclic ester intermediate. DMF was added to this intermediate and then heated at 135°C for 4 h to effect cyclization to oxadiazole. After cooling the reaction mixture was washed with water (3 times) and brine, dried over anhydrous sodium sulfate, filtered, and concentrated. Purification by flash column chromatography on silica gel

using 5% ethyl acetate in hexanes afforded the title compound 160 mg (12 % over 2 steps) as a white solid. m/z 244 (GCMS).

[0758] The following compounds were prepared analogously to Example 241:

Example No.	Name
242	3-Chloromethyl-5-(2,5-dichloro-thiophen-3-yl)-[1,2,4]oxadiazole
243	3-(3-Chloromethyl-[1,2,4]oxadiazol-5-yl)-benzonitrile
244	3-Chloromethyl-5-(3-fluoro-phenyl)-[1,2,4]oxadiazole
245	3-Chloromethyl-5-(2-methyl-thiazol-4-yl)-[1,2,4]oxadiazole
246	3-Chloromethyl-5-(4-fluoro-phenyl)-[1,2,4]oxadiazole
247	5-(5-Bromo-2-fluoro-phenyl)-3-chloromethyl-[1,2,4]oxadiazole
248	3-Chloromethyl-5-(4-methyl-thiophen-2-yl)-[1,2,4]oxadiazole
249	5-(3-chloromethyl-[1,2,4]oxadiazol-5-yl)-thiophene-3-carbonitrile
250	2-(3-Chloromethyl-[1,2,4]oxadiazol-5-yl)-4-methyl-benzonitrile
251	3-(3-Chloromethyl-[1,2,4]oxadiazol-5-yl)-5-fluoro-benzonitrile
252	3-(3-Chloromethyl-[1,2,4]oxadiazol-5-yl)-4-fluoro-benzonitrile
253	4-Chloro-2-(3-chloromethyl-[1,2,4]oxadiazol-5-yl)-phenol
254	3-(1-Chloro-ethyl)-5-(3-chloro-phenyl)-[1,2,4]oxadiazole
255	3-(1-Chloro-ethyl)-5-(3-fluoro-phenyl)-[1,2,4]oxadiazole
256	3-(1-Chloro-ethyl)-5-(5-chloro-2-fluoro-phenyl)-[1,2,4]oxadiazole

[0759] Example 257

[0760] [3-(3-Chloromethyl-[1,2,4]oxadiazol-5-yl)-phenyl]-methanol

[0761] 3-Hydroxymethylbenzoic acid, described in Reed, G. A.; Dimmel, D.R.; Malcolm, E. W. J. Org. Chem. 1993, 58 (23), 6372-6376, (175 mg, 1.15 mmol), 2-chloro-N-hydroxy-acetamidine (125 mg, 1.15 mmol) and HBTU was dissolved in anhydrous DMF (4 ml). Triethylamine (0.48 ml, 3.5 mmol) was added and the reaction was stirred at ambient temperature over night. The crude product was partitioned between dichloromethane and $NaHCO_3$ (aq), the organic phase was dried ($MgSO_4$) and the dichloromethane was removed in vacuo. The resulting DMF-solution was heated at 120 °C over night. The reaction mixture was concentrated in vacuo and the title compound (64 mg, 25%) was isolated by flash chromatography using 25-50% ethyl acetate in heptane. 1H NMR (CDCl3), δ (ppm): 8.15 (s, 1H), 8.06 (d, 1H), 7.62 (d, 1H), 7.53 (t, 1H); 4.80 (d, 2H), 4.66 (s, 1H); 1.99 (br. t, 1H).

[0762] The following compounds were prepared analogously to Example 257:

Example No.	Name
258	3-Chloromethyl-5-[1-(toluene-4-sulfonyl)-1H-pyr rol-3-yl]-[1,2,4]oxadiazole
259	3-Chloromethyl-5-furan-3-yl-[1,2,4]oxadiazole
260	3-Chloromethyl-5-(5-chloro-thiophen-2-yl)-[1,2,4]oxadiazole

[0763] Example 261

[0764] 1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethanol

[0765] Step 1: 1-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethoxy}-1H-benzotriazole: 2-(1-Chloro-ethyl)-5-(3-chloro-phenyl)-[1,3,4]oxadiazole (109 mg, 0.45 mmol), hydroxybenzotriazole (76.4 mg, 0.56 mmol) and potassium iodide (23.0 mg, 0.14 mmol) were dissolved in DMF (2.5 ml), followed by the addition of potassium carbonate (74.0 mg, 0.53 mmol). After stirring under argon at ambient temperatures for 24 h the reaction mixture was diluted with ethyl acetate and washed with 2N ammonium chloride solution. After reextraction of the aqueous layer with ethyl acetate, the combined organic layers were washed with brine and evaporated to

dryness. Column chromatography over 12 g silica using heptane / ethyl acetate = 4/1 gave after drying in vacuo the title compound (129 mg, 84%). 1H NMR ($CDCl_3$), δ (ppm): 7.94 (d, 1 H), 7.82 (m, 1 H), 7.76 (m, 1 H), 7.46 (m, 1 H), 7.39-7.27 (m, 4 H), 5.98 (q, 1 H), 2.04 (d, 3 H). Step 2: 1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethanol: 1-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethoxy}-1H-benzotriazole (58.4 mg, 0.17 mmol) was dissolved under argon in dry THF (3 ml). To this mixture a 0.1 molar solution of samarium diiodide in THF (5 ml, 0.5 mmol) was slowly added over 20 min. After stirring for 80 min additional samarium diioide solution (4 ml, 0.4 mmol) was added during 5 min. The reaction mixture was quenched after further 15 min of stirring with aqueous $Na_2S_2O_3$, diluted with diethyl ether and washed with 1 molare aqueous hydrochloric acid, dried over sodium sulfate and evaporated to dryness. After drying in vacuo crude title compound was obtained (36.0 mg, 92%) which was used in the next step without further purification. 1H NMR ($CDCl_3$), δ (ppm): 7.98-7.75 (m, 2 H), 7.50-7.38 (m, 2 H), 5.25 (q, 1 H), 1.74 (d, 3 H).

[0766] The following compounds were prepared analogously to Example 261:

Example No.	Name
262	[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-yl]-methanol

[0767] Example 263

[0768] 1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethanol

[0769] To a solution of 3.19 g (30.6 mmol) 2,N-dihydroxy-propionamidine in 25 ml pyridine was added 4.3 ml (33.7 mmol) 3-chloro-benzoyl chloride at 0°C. Cooling was removed and the mixture was stirred at room temperature for 25 min and at reflux for 25 min. After cooling the mixture was poured into water and extracted twice with CH_2Cl_2. The organic phase was dried and concentrated. Recrystallization from heptane/EtOAc afforded 4.12 g (60%) of a white solid. 1H NMR ($CDCl_3$), d (ppm): 1.68 (d, 3 H) 2.67 (m, 1 H) 5.09 (m, 1 H) 7.46 (t, 1 H) 7.56 (d, 1 H) 8.01 (d, 1 H) 8.13 (s, 1 H).

[0770] Example 264

[0771] [5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-methanol

[0772] Step 1: N-{4-[(Z)-{[5-(3-chlorophenyl)-1,2,4-oxadiazol-3-yl]methylene}(oxido)amino]phenyl}-N,N-dimethylamine: The title compound was synthesized according to the method described in Palazzo et al. J. Heterocycl. Chem. (1979) 16:1469. 1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethyl]-pyridinium chloride (1.81 g, 5.87 mmol) was dissolved in water (20 ml). To this solution, 4-nitroso-N,N-dimethylanilin (0.88 g, 5.86 mmol) dissolved in ethanol (50 ml) was added, followed by slow addition of 1 molar aq. sodium hydroxide (5.9 ml, 5.9 mmol) over a 3 min period. After 1 h the formed precipitate was filtered, washed with water and air-dried to give the title compound (2.08 g, wet) which was used immediately in the next step MS (ESI) m/z 344 (M+1). Step 2: [5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-methanediol: N-{4-[(Z)-{[5-(3-Chlorophenyl)-1,2,4-oxadiazol-3-yl]methylene}(oxido)amino]phenyl}-N,N-dimethylamine (2.08 g wet) was suspended in diethyl ether (30 ml), followed by the addition of 1 molar aqueous hydrochloric acid. The mixture was stirred vigorously for 20 min, transferred to a separation funnel and diluted with diethyl ether and 1 molar aqueous hydrochloric acid. After extraction, the aqueous layer was extracted two more times with diethyl ether. Combining the organic layers, drying over magnesium sulfate, followed by evaporation to dryness and drying in vacuo gave the title compound as crude (0.56 g, 42% from 1-[5-(3-chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethyl]-pyridinium chloride). MS (ESI) m/z 227 (M+1). Step 3: [5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-methanol: Step 3: [5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-methanol: 1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethyl]-pyridinium chloride (99.3 mg, 0.44 mmol) was dissolved in methanol (4 ml) followed by the addition of sodium borohydride (32 mg, 0.84 mmol). More sodium borohydride was added after 2 h and the reaction was allowed to run over night. The reaction mixture was diluted with dichloromethane and aq. ammonium chloride and stirred vigorously. After separation of the layers and washing of the organic layer with brine, followed by evaporation to dryness, crude product was obtained. This was purified by flash chromatography using heptane/ethyl acetate which gave the title compound (32.0 mg, 32%). 1H NMR ($CDCl_3$), δ (ppm): 8.11 (s, 1H), 8.00 (apparent d, 1H), 7.56 (apparent d, 1H), 7.46

(apparent t, 1H), 4.87 (d, 2H), 2.91 (t, 1H).

[0773] Example 265

[0774] 2-Chloromethyl-5-(2-fluoro-5-methyl-phenyl)-[1,3,4]oxadiazole

[0775] 2-Fluoro-5-methyl-benzoic acid hydrazide (320 mg, 1.9 mmol) and 2-chloro-1,1,1-triethoxy-ethane (1.9 ml) were heated in a sealed vial at 120°C for 30 min. The reaction mixture was place directly onto a flash column (silica gel) and purified by using 0 - 5% ethyl acetate in hexanes to afford 2-chloromethyl-5-(2-fluoro-5-methyl-phenyl)-[1,3,4]oxadiazole (284.5 mg, 66%). 1H NMR (CDCl3) d (ppm): 7.89 (q, 1H), 7.36 (m, 1H), 7.16 (t, 1H), 4.81 (s, 2H), 2.43 (s, 3H).

[0776] The following compounds were prepared analogously to Example 265:

Example No.	Name
266	2-Chloromethyl-5-(3-chloro-phenyl)-[1,3,4]oxadiazole
267	4-(5-Chloromethyl-[1,3,4]oxadiazol-2-yl)-2-methyl-pyridine
268	2-Chloromethyl-5-m-tolyl-[1,3,4]oxadiazole
269	3-(5-Chloromethyl-[1,3,4]oxadiazol-2-yl)-benzonitrile
270	2-Chloro-4-(5-chloromethyl-[1,3,4]oxadiazol-2-yl)-pyridine
271	2-(5-Chloro-2-fluoro-phenyl)-5-chloromethyl-[1,3,4]oxadiazole

[0777] Example 272

[0778] **2-(1-Bromo-ethyl)-5-(3-chloro-phenyl)-[1,3,4]oxadiazole**

[0779] 3-Chloro-benzoic acid hydrazide (170 mg, 1 mmol) and 2-bromo-1,1,1-triethoxypropane (1 ml) were heated in a sealed vial at 120°C for 10 min. The reaction mixture was place directly onto a flash column (silica gel) and purified using 0 – 50% dichloromethane in hexanes. The product was re-purified by flash column chromatography using a mixture of ethyl acetate:hexanes:dichloromethane

(1:19:20) to afford 2-(1-bromo-ethyl)-5-(3-chloro-phenyl)-[1,3,4]oxadiazole (93 mg, 32%, colorless oil). 1H NMR ($CDCl_3$) d (ppm): 8.09 (t, 1H), 7.99 (t, 1H), 7.55 (m, 3H), 5.30 (m, 1H), 2.21 (q, 3H).

[0780] The following compounds were prepared analogously to Example 272:

Example No.	Name
273	2-(1-Bromo-ethyl)-5-(5-chloro-2-fluoro-phenyl)-[1,3,4]oxadiazole
274	4-[5-(1-Bromo-ethyl)-[1,3,4]oxadiazol-2-yl]-2-methyl-pyridine
275	2-(1-Bromo-ethyl)-5-(2-fluoro-5-methyl-phenyl)-[1,3,4]oxadiazole
276	2-(1-Bromo-ethyl)-5-(3-chloro-phenyl)-[1,3,4]oxadiazole

[0781] Example 277

[0782] 3-(1-Bromo-ethyl)-5-(3-chloro-phenyl)-[1,2,4]oxadiazole

[0783] A solution of 396 mg (2.22 mmol) N-bromosuccinimid in 2 ml THF was added dropwise to a solution of 583 mg (2.22 mmol) triphenylphosphine in 2 ml THF at 0°C. After stirring for 20 min 416 mg (1.85 mmol) 1-[5-(3-chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethanol in 2 ml THF was added. Stirring was continued overnight at room temperature before the solvent was removed under reduced pressure. Flash chromatography (heptane/EtOAc 6:1) afforded 168 mg (32%). 1H NMR ($CDCl_3$), d (ppm): 2.12 (d, 3 H) 5.21 (q, 1 H) 7.47 (t, 1 H) 7.57 (m, 1 H) 8.03 (d, 1 H) 8.15 (s, 1 H).

[0784] Example 278

[0785] 1-[5-(3-Chloro-phenyl)-isoxazol-3-yl]-ethanol

[0786] Step 1 4-(3-Chloro-phenyl)-2,4-dioxo-butyric acid ethyl ester: Sodium hydride (60% oil dispersion, 1.24 g, 31.1 mmol) was added in portions to a solution of 3-chloroacetophenone (4.0 g, 25.9 mmol) and diethyl oxalate (4.54 g, 31.1 mmol) in DMF (32 ml) at 0°C. The mixture stirred at room temperature for 1 h and was then heated at 80°C for a half an h. After cooling, the mixture was treated with 3N HCl and

then diluted with ethyl acetate. The organic layer was washed with water (3X) and saturated brine, dried over anhydrous sodium sulfate, filtered and concentrated. The resulting residue was then purified by flash column chromatography on silica using 0 – 10% ethyl acetate in hexanes to afford of 4-(3-chloro-phenyl)-2,4-dioxo-butyric acid ethyl ester (4.43g, 67%, yellow solid). 1H NMR ($CDCl_3$) d (ppm): 15.12 (br s, 1H), 7.98 (s, 1H), 7.88 (d, 1H), 7.58 (d, 1H), 7.47 (t, 1H), 7.05 (s, 1H), 4.39 (m, 2H), 1.41 (m, 3H). Step 2: 5-(3-Chloro-phenyl)-isoxazole-3-carboxylic acid ethyl ester: A solution of 4-(3-chloro-phenyl)-2,4-dioxo-butyric acid ethyl ester (3.0 g, 11.8 mmol) and hydroxylamine hydrochloride (2.46 g, 35.4 mmol) in methanol (60 ml) was heated at 80°C for 4 h. After cooling, the mixture was filtered and washed with cold methanol to afford 5-(3-chloro-phenyl)-isoxazole-3-carboxylic acid ethyl ester (2.0 g, 71%, white solid). 1H NMR ($CDCl_3$) d (ppm): 7.82 (s, 1H), 7.72 (m, 1H), 7.47 (m, 2H), 4.03 (s, 3H). Mixture of both methyl and ethyl ester (mostly methyl). Step 3: 1-[5-(3-Chloro-phenyl)-isoxazol-3-yl]-ethanone: In a screw cap vial equipped with stir bar added methyl magnesium iodide (3M in diethyl ether) (0.79 ml, 2.38 mmol), toluene (1 ml), tetrahydrofuran (0.39 ml, 4.77 mmol) and triethylamine (1 ml, 7.15 mmol). Cooled the solution down to 0°C and to it added solution of 5-(3-chloro-phenyl)-isoxazole-3-carboxylic acid ethyl ester (300 mg, 1.19 mmol) in toluene (5 ml). Left the resulting mixture stirring at 0°C for 5 h. Reaction mixture was quenched with 1N hydrochloric acid (aqueous, 6.5 ml, 6.5 mmol), diluted with toluene (35 ml), sequentially washed with water (50 ml), saturated sodium bicarbonate (aqueous, 30 ml), water (50 ml) and brine (30 ml). The organic phase was concentrated, in-vacuo. The isolated residue was dissolved in methanol (8 ml) and 20% potassium hydroxide (aqueous, 1 ml). The mixture was stirred at 45°C for 30 min. At this point the mixture was concentrated, in-vacuo. The isolated residue was dissolved in toluene (60 ml), sequentially washed with water (50 ml), saturated sodium bicarbonate (aqueous, 50 ml) and water (50 ml). The organic phase was concentrated, in-vacuo. The crude residue was purified on silica gel using 2% ethyl acetate in hexanes to isolate the desired compound as a white solid (156 mg, 60%). 1H-NMR ($CDCl_3$), d (ppm): 7.77 (m, 1H), 7.66 (m, 1H), 7.42 (m, 2H), 6.90 (s, 1H), 2.69 (s, 3H). Step 4: 1-[5-(3-Chloro-phenyl)-isoxazol-3-yl]-ethanol: In a screw cap vial equipped with stir bar

added 1-[5-(3-chloro-phenyl)-isoxazol-3-yl]-ethanone (100 mg, 0.45 mmol), sodium borohydride (34 mg, 0.90 mmol) and methanol (3 ml). Left the resulting mixture stirring at room temperature for 3 h. Reaction was quenched with water (30 ml) and brine (30 ml), extracted with dichloromethane (3X30 ml). Combined organic phase was dried (sodium sulfate), filtered and concentrated, in-vacuo to isolate 1-[5-(3-Chloro-phenyl)-isoxazol-3-yl]-ethanol as a white solid (110 mg). 1H-NMR (CDCl3), d (ppm): 7.69 (m, 1H), 7.59 (m, 1H), 7.37 (m, 2H), 6.59 (s, 1H), 5.07 (q, 1H), 3.45 (bs, 1H), 1.58 (d, 3H).

[0787] The following compound was prepared analogously to Example 278:

Example No.	Name
279	1-[5-(2-Fluoro-5-methyl-phenyl)-isoxazol-3-yl]-ethanol

[0788] The following compounds were prepared analogously to 5-(3-Chloro-phenyl)-isoxazole-3-carboxylic acid ethyl ester (step 2 in the synthesis of Example 279):

Example No.	Name
280	5-(2-Fluoro-5-methyl-phenyl)-isoxazole-3-carboxylic acid methyl ester
281	5-Thiophen-3-yl-isoxazole-3-carboxylic acid methyl ester
282	5-Phenyl-isoxazole-3-carboxylic acid methyl ester
283	5-(3-Chloro-phenyl)-4-methyl-isoxazole-3-carboxylic acid ethyl ester
284	5-(5-Chloro-thiophen-3-yl)-isoxazole-3-carboxylic acid methyl ester

[0789] Example 285

[0790] [5-(3-Chloro-phenyl)-isoxazol-3-yl]-methanol

[0791] Lithium aluminum hydride (320 mg, 8.4 mmol) was slowly added to a solution of 5-(3-chloro-phenyl)-isoxazole-3-carcoxylic acid ethyl ester (2.0 g, 8.4) in THF (100 ml) at room temperature. After 1 h, the reaction mixture was quenched

with water and then extracted with ethyl acetate. The organic layer was washed with water and saturated brine, dried over anhydrous sodium sulfate, filtered, and concentrated. The resulting residue was then purified by flash column chromatography using 15-40% ethyl acetate in hexane to afford [5-(3-chloro-phenyl)-isoxazol-3-yl]-methanol (1.32g, 75%, yellow solid). 1H NMR ($CDCl_3$) d (ppm): 7.78 (s, 1H), 7.68 (m, 1H), 7.43 (m, 2H), 6.63 (s, 1H), 4.84 (d, 2H), 2.23 (t, 1H).

[0792] The following compounds were prepared analogously to Example 285:

Example No.	Name
286	[2-(3-Chloro-phenyl)-oxazol-4-yl]-methanol
287	[3-(3-Chloro-phenyl)-isoxazol-5-yl]-methanol
288	5-(Thiophen-3-yl-isoxazol-3-yl)methanol
289	[5-(2-Fluoro-5-methyl-phenyl)-isoxazol-3-yl]-methanol
290	(5-Phenyl-isoxazol-3-yl)-methanol
291	[5-(3-Chloro-phenyl)-4-methyl-isoxazol-3-yl]-methanol
292	[5-(5-Chloro-thiophen-3-yl)-isoxazol-3-yl)]-methanol

[0793] Example 293

[0794] Methanesulfonic acid 1-[5-(3-Chloro-phenyl)-isoxazol-3-yl]-ethyl ester

[0795] In a screw cap vial equipped with stir bar was added 1-[5-(3-chloro-phenyl)-isoxazol-3-yl]-ethanol (110 mg, 0.49 mmol), dichloromethane (3 ml) and triethylamine (0.34 ml, 2.46 mmol). Cooled the mixture down to 0°C and to it added methane sulfonyl chloride (0.08 ml, 0.98 mmol). Left the reaction mixture stirring at room temperature for 30 min. Reaction was quenched with saturated sodium bicarbonate (aqueous, 40 ml) and extracted with dichloromethane (3X30 ml). Combined organic phase was washed with brine (40 ml), dried (sodium sulfate), filtered and concentrated, in-vacuo to isolate the desired compound as brown oil.

[0796] The following compounds were prepared analogously to Example 293:

Example No.	Name

294	Methanesulfonic acid 2-(3-chloro-phenyl)-oxazol-4-ylmethyl ester
295	Methanesulfonic acid 3-(3-chloro-phenyl)-isoazol-5-ylmethyl ester
296	Methanesulfonic acid 5-(2-fluoro-5-methyl-phenyl)-isoxazol-3-ylmethyl ester
297	Methanesulfonic acid -phenyl)-isoxazol-5-yl]-ethyl ester
298	Methanesulfonic acid 5-(5-chloro-2-fluoro-phenyl)-isoxazol-3-ylmethyl ester
299	Methanesulfonic acid 5-(3-chloro-phenyl)-isoxazol-3-ylmethyl ester
300	Methanesulfonic acid 5-thiophen-3-yl-isoxazol-3-ylmethyl ester
301	Methanesulfonic acid 5-(2-fluoro-5-methyl-phenyl)-isoxazol-3-ylmethyl ester
302	Methanesulfonic acid 5-phenyl-isoxazol-3-ylmethyl ester
303	Methanesulfonic acid 5-(3-chloro-phenyl)-4-methyl-isoxazol-3-ylmethyl ester
304	Methanesulfonic acid 5-(5-chloro-thiophen-3-yl)-isoxazol-3-ylmethyl ester
305	Methanesulfonic acid 1-[5-(2-fluoro-5-methyl-phenyl)-isoxazol-3-yl]-ethyl ester
306	Methanesulfonic acid 1-[5-(5-chloro-2-fluoro-phenyl)-isoxazol-3-yl]-ethyl ester

[0797] Example 307

[0798] Methanesulfonic acid 4-chloro-5-(3-chloro-phenyl)-isoxazol-3-ylmethyl ester

[0799] Sulfuryl chloride (1 ml) was added to methanesulfonic acid 5-(3-chloro-phenyl)-isoxazol-3-ylmethyl ester (200 mg, 0.70 mmol) and then stirred at 60°C overnight. The reaction mixture was diluted with dichloromethane, washed saturated sodium bicarbonate, dried over anhydrous sodium sulfate, filtered and concentrated to afford methanesulfonic acid 4-chloro-5-(3-chloro-phenyl)-isoxazol-3-ylmethyl ester (219 mg,, 97%, light brown solid). 1H NMR ($CDCl_3$) d (ppm): 8.07 (m, 1H), 7.92 (m,

1H), 7.50 (m, 2H), 5.38 (s, 2H), 3.16 (s, 3H).

[0800] Example 308

[0801] 3-(3-Chloro-phenyl)-isoxazole-5-carboxylic acid methyl ester

[0802] Step 1: 3-Chloro-N-hydroxy-benzamidine: A solution of 3-chlorobenzaldehyde (3.35 ml, 0.030 mmol) in ethanol (40 ml) was added to a solution of hydroxylamine hydrochloride (2.47 g, 0.036 mmol) and sodium hydroxide (1.42 g, 0.036) in water (20 ml) at room temperature and then heated at 90°C for 24 h. After cooling, the reaction mixture was concentrated, the residue diluted with water and then the precipitate was filtered and dried to afford 3-chloro-N-hydroxy-benzamidine (1.13 g, 93 %). 1H NMR ($CDCl_3$) d (ppm): 8.11 (s, 1H), 7.72 (s, 1H), 7.61 (m, 1H), 7.46 (m, 1H), 7.36 (m, 1H). Step 2: 3-Chloro-N-hydroxy-benzimidoyl chloride: N-chlorosuccinimide (858 mg, 6.4 mmol) was added to a solution of 3-chloro-N-hydroxy-benzamidine (1 g, 6.4 mmol) at room temperature and stirred for 1 h. The reaction mixture was diluted with diethyl ether and then washed with water (3X), dried over anhydrous magnesium sulfate, filtered, and concentrated to afford the titled compound (1.13 g, 93 %). 1H NMR ($CDCl_3$) d (ppm): 8.03 (s, 1H), 7.87 (m, 1H), 7.76 (m, 1H), 7.43 (m,1H).: Step 3: 3-(3-Chloro-phenyl)-isoxazole-5-carboxylic acid methyl ester: Triethyl amine (0.73 ml, 5.3 mmol) was added drop-wise to a solution of 3-chloro-N-hydroxy-benzimidoyl chloride (1.0 g, 5.3 mmol) and methyl propiolate (2.2 ml, 25.3 mmol) in an ice-bath. The reaction mixture was warmed to room temperature and left to stir overnight. After diluting the reaction with dichloromethane, the organic layer was washed with water and saturated brine, dried over anhydrous sodium sulfate, filtered, and concentrated. Purification by flash column chromatography eluted with 50% hexanes in ethyl acetate and then recrystallization with methanol afforded 3-(3-chloro-phenyl)-isoxazole-5-carboxylic acid methyl ester (635 mg, 51%, white solid). 1H NMR ($CDCl_3$) d (ppm): 7.86 (m, 1H), 7.74 (m, 1H), 7.46 (2H), 7.2 (s, 1H), 4.05 (s, 3H).

[0803] Example 309

[0804] 2-Bromomethyl-5-(3-chloro-phenyl)-oxazole

[0805] Step 1 5-(3-Chloro-phenyl)-2-methyl-oxazole: To a solution of Tl(OAc)3 (4.2 g, 11.1 mmol) in acetonitrile (80 ml), trifluoromethanesulfuric acid (5g, 33.3 mmol) was added dropwise at room temperature and stirred for 15 min. The reaction mixture was then heated to 80°C and 1-(3-chloro-phenyl)-ethanone (1.14 g, 7.4 mmol) in acetonitrile (40 ml) was added. After one h, the reaction was quenched with dichloromethane and saturated sodium bicarbonate. The organic layer was dried, purified by column chromatography with 5~19 % ethyl acetate in hexanes to give 1.2 (83.9 %) g of 5-(3-chloro-phenyl)-2-methyl-oxazole as yellow oil. 1H-NMR($CDCl_3$) d(ppm): 7.60 (s, 1H), 7.48 (d, 1H), 7.29 (m, 2H), 7.23 (s, 1H) and 2.34 (s, 3H). Step 2: 2-Bromomethyl-5-(3-chloro-phenyl)-oxazole: 5-(3-chloro-phenyl)-2-methyl-oxazole (580 mg, 3 mmol) was mixed with NBS (531 mg, 3 mmol) and BPOA (36.3 mg, 0.15 mmol) in CCl_4 at room temperature. The reaction mixture was heated at 75 °C for 2 h and then quenched with water and dichloromethane. The organic layer was dried, concentrated, purified by column chromatography with 2~5 % ethyl acetate in hexanes to give 562 mg (68.3 %) of 2-bromomethyl-5-(3-chloro-phenyl)-oxazole as yellow oil. 1H-NMR($CDCl_3$) d(ppm): 7.67 (s, 1H), 7.54 (d, 1H), 7.35(m, 3H) and 4.56 (s, 2H).

[0806] Example 310

[0807] 2-(3-Chloro-phenyl)-oxazole-4-carboxylic acid methyl ester

[0808] To a mixture of 3-Chlorobenzoic acid (5.0 g, 31.9 mmol), serine methylester hydrochloride (6.1 g, 31.9 mmol) and HOBt (4.31 g, 31.9 mmol) in DMF (100 ml) was added N-methylmorpholine (NMM) (7.0 ml, 63.8 mmol) and EDCI (4.97 g, 31.9 mmol) at 0°C. The mixture was allowed to warm to room temperature and stirred for 18 h. The mixture was diluted with ethyl acetate (300 ml) and then washed with water (3 x 250 ml) followed by brine. The organic extract was dried over Na_2SO_4 (anhydrous) and then concentrated in vacuo giving 2-(3-Chloro-benzoylamino)-3-hydroxy-propionic acid methyl ester (7.2 g, 93%) of a pale yellow solid. 1H NMR ($CDCl_3$) d (ppm): 7.78 (s, 1 H), 7.66 (d, 1 H), 7.45, (dd, 1 H), 7.34 (t, 1 H), 7.25 (br, d, 1H), 4.82 (m, 1 H), 4.08 (m, 2 H), 3.79 (s, 3 H), 3.19 (br, t, 1H).

[0809] To a solution of 2-(3-chloro-benzoylamino)-3-hydroxy-propionic acid

methyl ester (7.2 g, 29.6 mmol) in CH_2Cl_2 at -20°C was added dropwise De-oxofluor (7.2 g, 32.6 mmol). After stirring at this temperature for 30 min, $BrCCl_3$ (3.6 g, 18.1 mmol) was added dropwise followed by DBU (2.79g, 18.1 mmol). The mixture was then stirred at 2-3°C for 8 h ad then quenched with saturated $NaHCO_3$ followed by extraction with ethyl acetate. The organic extract as then washed with brine and dried over Na_2SO_4 (anhydrous). Purification was performed by flash column chromatography on silica gel using ethyl acetate in hexanes as eluant to afford 2-(3-chloro-phenyl)-oxazole-4-carboxylic acid methyl ester (4.1g, 59%) as a yellow solid. 1H NMR ($CDCl_3$) d (ppm): 8.30 (s, 1 H), 8.12 (d, 1 H), 7.98 (dd, 1 H), 7.45 (m, 2 H), 3.96 (s, 3 H).

[0810] Example 311

[0811] 2-(3-Chloro-phenyl)-oxazole-4-carboxylic acid methyl ester

[0812] To a mixture of 3-Chlorobenzoic acid (5.0 g, 31.9 mmol), serine methylester hydrochloride (6.1 g, 31.9 mmol) and HOBt (4.31 g, 31.9 mmol) in DMF (100 ml) was added N-methylmorpholine (NMM) (7.0 ml, 63.8 mmol) and EDCI (4.97 g, 31.9 mmol) at 0°C. The mixture was allowed to warm to room temperature and stirred for 18 h. The mixture was diluted with ethyl acetate (300 ml) and then washed with water (3 x 250 ml) followed by brine. The organic extract was dried over Na_2SO_4 (anhydrous) and then concentrated in vacuo giving 2-(3-Chloro-benzoylamino)-3-hydroxy-propionic acid methyl ester (7.2 g, 93%) of a pale yellow solid. 1H NMR ($CDCl_3$) d (ppm): 7.78 (s, 1 H), 7.66 (d, 1 H), 7.45, (dd, 1 H), 7.34 (t, 1 H), 7.25 (br, d, 1H), 4.82 (m, 1 H), 4.08 (m, 2 H), 3.79 (s, 3 H), 3.19 (br, t, 1H).

[0813] To a solution of 2-(3-chloro-benzoylamino)-3-hydroxy-propionic acid methyl ester (7.2 g, 29.6 mmol) in CH_2Cl_2 at -20°C was added dropwise De-oxofluor (7.2 g, 32.6 mmol). After stirring at this temperature for 30 min, $BrCCl_3$ (3.6 g, 18.1 mmol) was added dropwise followed by DBU (2.79g, 18.1 mmol). The mixture was then stirred at 2-3°C for 8 h ad then quenched with saturated $NaHCO_3$ followed by extraction with ethyl acetate. The organic extract as then washed with brine and dried over Na_2SO_4 (anhydrous). Purification was performed by flash column chromatography on silica gel using ethyl acetate in hexanes as eluant to afford 2-(3-

chloro-phenyl)-oxazole-4-carboxylic acid methyl ester (4.1g, 59%) as a yellow solid. 1H NMR ($CDCl_3$) d (ppm): 8.30 (s, 1 H), 8.12 (d, 1 H), 7.98 (dd, 1 H), 7.45 (m, 2 H), 3.96 (s, 3 H).

[0814] Example 312

[0815] 1-[5-(5-Chloro-2-fluoro-phenyl)-isoxazol-3-yl]-ethanol

[0816] Step 1: 5-(5-Chloro-2-fluoro-phenyl)-isoxazole-3-carbaldehyde: In a 50 ml round bottom flask equipped with stir bar and drying tube added 5-(5-chloro-2-fluoro-phenyl)-isoxazole-3-carboxylic acid ethyl ester (0.78 g, 2.89 mmol) and dichloromethane (10 ml). Cooled the solution down to –78°C and to this stirred solution added diisobutylaluminum hydride (1M hexanes, 5.3 ml, 5.3 mmol). The resulting mixture was left stirring at –78°C for 3 h. Reaction was quenched using sodium sulfate decahydrate. The resulting mixture was stirred at 63°C for 15 min after which it was filtered through a celite pad. The filterate was concentrated in-vacuo to isolate an off-white solid, which was triturated with hexanes to isolate the title compound as a white solid (0.55g, 84%). 1H-NMR ($CDCl_3$), d (ppm): 10.2 (s, 1H), 7.99 (m, 1H), 7.44 (m, 1H), 7.20 (m, 1H), 7.10 (d, 1H). Step 2: 1-[5-(5-Chloro-2-fluoro-phenyl)-isoxazol-3-yl]-ethanol: In a 50 ml round bottom flask equipped with stir bar added 5-(5-chloro-2-fluoro-phenyl)-isoxazole-3-carbaldehyde (0.55 g, 2.42 mmol) and tetrahydrofuran (6 ml). Cooled the mixture down to 0°C and to it added methyl magnesium iodide (3M in diethyl ether, 3.23 ml, 9.67 mmol). The resulting mixture was left stirring at 0°C for 3 h. Reaction mixture was quenched with hydrochloric acid (1N, aqueous, 10 ml), extracted with diethyl ether (3X50 ml). Combined organic phase was washed with water (50 ml), brine (50 ml), dried (sodium sulfate), filtered and concentrated in-vacuo. The crude residue was purified on silica gel using 10% ethyl acetate in hexanes to isolate the desired compound as clear oil (179 mg, 31%).

[0817] Example 313

[0818] 1-[3-(3-Chloro-phenyl)-isoxazol-5-yl]-ethanol

[0819] 3-Chloro-benzohydroximoyl chloride (e.g. Kim, Jae Nyoung; Ryu, Eung K;

J. Org. Chem. (1992), 57(24), 6649-50) (2.84 g, 14.8 mmol) was suspended in benzene (50 ml) and cooled to 0°C. 3-Butyn-2-ol (2.10 g, 29.9 mmol) and triethylamine (1.89 ml, 26.7 mmol) were added. The mixture was heated to 60°C for 1.5 houes, cooled and diluted with benzene and 1N aqueous hydrochloric acid. After stirring, the separated benzene layer was evaporated to dryness and the crude purified via flash chromatography over silica using heptane/ethyl acetate = 5/1 giving after drying in vacuo the title compound (0.49 g, 15%). 1H NMR ($CDCl_3$), δ (ppm): 1.64 (d, 3 H), 5.07 (dq, 1 H), 6.50 (s, 1 H), 7.40 (m, 2 H), 7.68 (m, 1 H), 7.79 (m, 1 H)

[0820] Example 314

[0821] [5-(5-Chloro-2-fluoro-phenyl)-isoxazol-3-yl]-methanol

[0822] Step 1: (5-Chloro-2-fluoro-phenylethynyl)-trimethyl-silane: In a 250 ml round bottom flask equipped with a stir bar and reflux condenser added 4-chloro-2-bromo-1-fluoro-benzene (5 g, 23.9 mmol), triphenylphosphine (250 mg, 0.10 mmol), (trimethylsilyl)acetylene (5.2 ml, 36.5 mmol)and triethylamine (60 ml). The reaction mixture was purged with argon, followed by addition of palladium (II) acetate (108 mg, 0.05 mmol). The resulting mixture was left stirring at reflux under argon, overnight. The reaction mixture was filtered through a pad of celite using ethyl acetate and the filterate was concentrated in-vacuo. The isolated residue was absorbed on silica gel and filtered using hexanes. The filterate was concentrated in-vacuo to isolate the title compound as brown oil (5.42 g). Step 2: 4-Chloro-2-ethynyl-1-fluoro-benzene: In a 250 ml round bottom flask equipped with stir bar added (5-chloro-2-fluoro-phenylethynyl)-trimethyl-silane (5.42 g, 23.9 mmol), potassium carbonate (16.5 g, 120 mmol) and methanol (60 ml). The reaction mixture was left stirring at room temperature for 1 h. Diluted the reaction mixture with hexanes (200 ml) and washed with water (250 ml). The aqueous phase was extracted with hexanes (2X100 ml). Combined organic phase was washed with brine (200 ml), dried (sodium sulfate), filtered and concentrated in-vacuo to isolate the desired compound as brown oil (3.56 g). 1H-NMR ($CDCl_3$), d (ppm): 7.47 (dd, 1H), 7.30 (m, 1H), 7.05 (t, 1H), 3.36 (s, 1H). Step 3: Chloro-hydroxyimino-acetic acid ethyl ester: In 1 L round bottom flask equipped with stir bar added amino-acetic acid ethyl ester hydrochloride (20 g, 143

mmol) and water (30 ml). The solution was cooled down to 0°C followed by sequential addition of concentrated hydrochloric acid (11.8 ml, 143 mmol) and dropwise addition of sodium nitrite (9.89 g, 143 mmol) solution in water (15 ml). After 10 min added another equivalent each of concentrated hydrochloric acid and sodium nitrite solution in water. The reaction mixture was left stirring at 0°C for 1 h. Reaction mixture was extracted with ether (4X100 ml). Combined organic phase was dried (sodium sulfate), filtered and concentrated in-vacuo to isolate a lemon yellow solid. The solid was recrystallized from hexanes to isolate a white solid (11 g, 51%). 1H-NMR ($CDCl_3$), d (ppm): 9.98 (bs, 1H), 4.40 (q, 2H), 1.38 (t, 3H). Step 4: 5-(5-Chloro-2-fluoro-phenyl)-isoxazole-3-carboxylic acid ethyl ester: In a 250 ml round bottom flask equipped with stir bar added 4-chloro-2-ethynyl-1-fluoro-benzene (2 g, 12.9 mmol), chloro-hydroxyimino-acetic acid ethyl ester (3.92 g, 25.9 mmol), sodium bicarbonate (7.07 g, 84.1 mmol) and toluene (50 ml). Reaction mixture was left stirring at room temperature for 48 h, after which it was concentrated in-vacuo. Residue was taken up in ethyl acetate (200 ml), sequentially washed with water (150 ml), brine (150 ml), dried (sodium sulfate), filtered and concentrated in-vacuo. The crude residue was purified on silica gel using 3% acetone in hexanes to isolate the title compound as an off-white solid (1.56 g). 1H-NMR ($CDCl_3$), d (ppm): 8.00 (dd, 1H), 7.43 (m, 1H), 7.18 (m, 2H), 4.51 (q, 2H), 1.47 (t, 3H). Step 5: [5-(5-Chloro-2-fluoro-phenyl)-isoxazol-3-yl]-methanol: In a 50 ml round bottom flask equipped with stir bar and drying tube added 5-(5-chloro-2-fluoro-phenyl)-isoxazole-3-carboxylic acid ethyl ester (0.78 g, 2.89 mmol) and tetrahydrofuran (10 ml). To this stirred solution added solution of lithium aluminum hydride (0.12 g, 2.89 mmol) in tetrahydrfuran (2 ml). The resulting mixture was left stirring at room temperature for 1 h. Reaction was quenched using sodium sulfate decahydrate. The resulting mixture was stirred at 63°C for 15 min after which it was filtered through a celite pad. The filterate was concentrated in-vacuo to isolate the title compound as yellow solid (0.65 g, 99%). 1H-NMR ($CDCl_3$), d (ppm): 7.73 (dd, 1H), 7.27 (m, 1H), 7.24 (t, 1H), 6.73 (d, 1H), 4.77 (s, 2H), 4.45 (bs, 1H).

[0823] Example 315

[0824] 3-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-propionic acid hydrazide

[0825] Step 1: 3-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-propionic acid: 3-Chloro-benzoic acid hydrazide (3.4 g, 20 mmol) and succinic anhydride (2. g, 20 mmol) was mixed in ethyl acetate (50 ml) at room temperature for 15 min. The reaction mixture was diluted with ether and the precipitate was filtered to give 5.1 g of 4-[N'-(3-chloro-benzoyl)-hydrazino]-4-oxo-butyric acid. 1H-NMR($CDCl_3$ + DMSO-d6) d(ppm): 10.01 (s, 1H), 9.53 (s, 1H), 7.68 (s, 1H), 7.55 (d, 1H), 7.21 (d, 1H), 7.12 (t, 1H) and 2.35 (m, 4H). This solid was mixed with conc. H_2SO_4 and stirred at room temperature for 45 min and the reaction mixture was carefully added to crashed ice (400g). The precipitate was filtered to give 4.07 g (80.6 %) of 3-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-propionic acid as white solid. 1H-NMR(DMSO-d6) d(ppm): 12.4 (w, 1H), 7.96 (s, 1H), 7.91 (d, 1H), 7.71 (d, 1H), 7.63 (t, 1H), 3.15 (t, 2H) and 2.82 (t, 2H). Step 2: 3-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-propionic acid hydrazide: 3-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-propionic acid (2.52 g, 10 mmol) was mixed with iodomethane (5.68 g, 40 mmol) and K_2CO_3 (5.52 g, 40 mmol) in DMF (25 ml) at room temperature overnight. The reaction mixture was diluted with ethyl acetate and washed with water 3 times, dried with $MgSO_4$ and concentrated to give 2.57 g of 3-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-propionic acid methyl ester. The methyl ester (2.54 g, 9.52 mmol) was mixed with 98% hydrazine hydrate (4.76 g, 95.2 mmol) in methanol (10 ml) for an h. The reaction mixture was concentrated, diluted with water, filtered to give 2.17 g (81.4 %) of 3-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-propionic acid hydrazide as white solid. 1H-NMR($CDCl_3$ + DMSO-d6) d(ppm): 8.75 (w, 1H), 7.91 (s, 1H), 7.82 (d, 1H), 7.42 (m, 2H), 3.45 (w, 2H), 3.19 (t, 2H) and 2.68 (t, 2H).

[0826] Example 316

[0827] 3-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-butyric acid hydrazide

[0828] Step 1: 2-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethyl}-malonic acid dimethyl ester: 2-(1-Chloro-ethyl)-5-(3-chloro-phenyl)-[1,3,4]oxadiazole (331 mg, 1.36 mmol) was mixed with dimethyl malonate (360 mg, 2/76 mmol) and DBU (207 mg, 1.36 mmol) in acetonitrile (3 ml) at 70 °C overnight. The reaction mixture

was dilute with dichloromethane and washed with water. The organic layer was dried and concentrated. The residue was purified with 5~20 % ethyl acetate in hexanes to give 357 mg (74.3 %) 2-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethyl}-malonic acid dimethyl ester as white solid. 1H-NMR($CDCl_3$) d(ppm): 8.03 (s, 1H), 7.95 (d, 1H), 7.53 (d, 1H), 7.47 (t, 1H), 4.06 (d, 1H), 3.95 (m, 1H), 3.84 (s, 3H), 3.74 (s, 3H) and 1.51 (d, 3H). Step 2: 3-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-butyric acid methyl ester: 2-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethyl}-malonic acid dimethyl ester (352.8 mg, 1.0 mmol) was mixed with sodium chloride (76.3 mg, 1.3 mmol) and a drop of water in DMSO (1.5 ml) at 175 °C for an h. The reaction mixture was diluted with water and extracted with dichloromethane. The organic layer was washed with water and concentrated. The residue was purified with column chromatography with 10~20 % ethyl acetate in hexanes to give 215 mg (76.8 %)3-[5-(3-chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-butyric acid methyl ester as clear oil. 1H-NMR($CDCl_3$) d(ppm): 8.03 (s, 1H), 7.94 (d, 1H), 7.53 (d, 1H), 7.45 (t, 1H), 3.73 (s, 3H), 3.67 (m, 1H), 3.05 (dd, 1H), 2.73 (dd, 1H) and 1.50 (d, 3H). Step 3: 3-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-butyric acid hydrazide: 3-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-butyric acid hydrazide (146 mg, %) was obtained from 3-[5-(3-chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-butyric acid methyl ester (215 mg, 0.766 mmol) reacted with hydrazine hydrate (0.74 ml) in methanol (3 ml) at room temperature for 2.5 h. 1H-NMR($CDCl_3$) d(ppm): 8.03 (s, 1H), 7.94 (d, 1H), 7.53 (d, 1H), 7.46 (t, 1H), 7.23 (w, 1H), 3.93 (w, 2H), 3.71 (m, 1H), 2.90 (dd, 1H), 2.57 (dd, 1H) and 1.50 (d, 3H).

[0829] Example 317

[0830] 3-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propionimidic acid ethyl ester hydrochloride

[0831] Step 1: 3-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propionamide: 3-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propionic acid (1.6 g, 6.33 mmol) was reacted with $SOCl_2$ (10 ml) at room temperature overnight. The reaction mixture was concentrated by vacuum. The residue was mixed with THF (20 ml) and quenched with 28 % $NH_3.H_2O$ (5 ml) at 0 °C. After being stirred for 2 h, the reaction mixture

was dilute with dichloromethane and washed with water and brine. The organic layer was dried, concentrate and triturated with hexanes to give 1.21 g (76 %) of 3-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propionamide. 1H-NMR($CDCl_3$) d(ppm): 8.07 (s, 1H), 7.96 (d, 1H), 7.45 (m, 2H), 5.60 (dw, 2H), 3.32 (t, 2H) and 2.87 (t, 2H). Step 2: 3-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propionitrile: 3-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propionamide (1.2 g, 4.77 mmol) was mixed with pyridine (0.829 g, 10.5 mmol) and trifluoroacetic anhydride (1.2 g, 5.72 mmol) in dichloromethane(25 ml) at room temperature for 2 h. The reaction mixture was diluted with dichloromethane and washed with water and brine. The organic layer was dried to give 1.1 g (98%) of 3-[3-(3-chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propionitrile as pale-brown oil. 1H-NMR($CDCl_3$) d(ppm): 8.09 (s, 1H), 7.98 (d, 1H), 7.45 (m, 2H), 5.60 (dw, 2H), 3.35 (t, 2H) and 3.01 (t, 2H). Step 3: 3-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propionimidic acid ethyl ester hydrochloride: 3-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propionitrile (1.1 g, 4.71 mmol) was mixed with 24 % HCl in ethanol (8 ml) overnight. The precipitate was filtered and washed with ether to give 0.99 g (66 %) of 3-[3-(3-chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propionimidic acid ethyl ester hydrochloride as white solid. 1H-NMR(DMSO-d6) d(ppm): 11.70 (w, 2H), 7.78 (m, 2H), 7.64 (m, 2H), 4.41 (q, 2H), 3.45 (t, 2H), 3.22 (t, 2H) and 1.28 (t, 3H).

[0832] Example 318

[0833] 3-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propionic acid hydrazide

[0834] Step 1: 3-[3-(3-chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propionic acid: 3-Chloro-N-hydroxy-benzamidine 4.52 g, 26.5 mmol) was heated with succinic anhydride (2.65 mg, 26.5 mmol) in DMF (5 ml) at 150°C for an h. The reaction mixture was cooled down and diluted with ethyl acetate. The organic solution was washed with water and brine, concentrated by vacuum. The residue was triturated with 20 % ethyl acetate in hexanes to give 4.0 g (60 %) of 3-[3-(3-chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propionic acid as white solid.). 1H-NMR($CDCl_3$) d(ppm): 8.08 (s, 1H), 7.96 (d, 1H), 7.49 (d, 1H), 7.42 (t, 1H), 3.28 (t, 2H) and 3.04 (t, 2H). Step 2: 3-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propionic acid hydrazide: This

acid was reacted with iodoethane (1.6g, 10.5 mmol) and K_2CO_3 (1.46 10.5 mmol) in DMF (5 ml) for 5 min to form 3-[3-(3-chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propionic acid ethyl ester. The ethyl ester was then treated with 37% hydrazine (2ml) in ethanol (5 ml) at 80 °C for2 h to give 595 mg (65% in 3 steps) of 3-[3-(3-chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propionic acid hydrazide as off-white solid1H-NMR($CDCl_3$) d(ppm): 8.07 (s, 1H), 7.96 (d, 1H), 7.49 (d, 1H), 7.43 (t, 1H), 7.00 (w, 1H), 3.95 (w, 2H), 3.34 (t, 2H) and 2.79 (t, 2H).

[0835] Example 319

[0836] [5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-acetic acid hydrazide

[0837] Step 1: (N-Hydroxycarbamimidoyl)-acetic acid ethyl ester: To a ethanol solution (40 ml) of cyano-acetic acid ethyl ester (9.9 g, 0.1 mol), the mixture solution of sodium hydroxide (4 g, 0.1 mol) in water (40 ml) and 5 M hydroxylamine hydrochloride (20 ml) was added and the reaction mixture was stirred at 50 °C overnight. After being concentrated, the reaction mixture was diluted with water and extrated with ethyl acetate. The organic layer was dried, concentrated again. The residue was purified by column chromatography with 30~70 % ethyl acetate in hexanes to give 3.32 g (22.7 %) of (N-Hydroxycarbamimidoyl)-acetic acid ethyl ester as white solid. 1H-NMR($CDCl_3$) d(ppm): 5.04 (ws, 2H), 4.20 (q, 2H), 3.19 (s, 2H) and 1.30 (t, 3H). Step 2: [5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-acetic acid ethyl ester: To a dichloromethane solution (10 ml) of (N-hydroxycarbamimidoyl)-acetic acid ethyl ester (1.46 g, 10 mmol) and triethylamine, 3-chlorobenzoyl chloride (1.75 g, 10 mmol) was added slowly at 5 °C and the reaction mixture was stirred for 10 min. DMF (8 ml) was added to the reaction mixture was heated to 135 °C for 2 h. Standard work-up, the product was passed column with dichloromethane to give 1.2 g (45 %) of [5-(3-chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-acetic acid ethyl ester as pale-yellow oil. 1H-NMR($CDCl_3$) d(ppm): 8.168 (s, 1H), 8.04 (d, 1H), 7.59 (d, 1H), 7.49 (t, 1H), 4.26 (q, 2H), 3.91 (s, 2H) and 1.31 (t, 3H). Step 3: [5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-acetic acid hydrazide: 5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-acetic acid ethyl ester (0.64 g, 2.4 mmol) was mixed with 37 % hydrazine (1.6 ml) in ethabol (10 ml) at 80 °C for 4 h. The reaction mixture was concentrated and diluted

with water. The precipitate was filtered, washed with water to give 0.51 g (83.3 %) of [5-(3-chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-acetic acid hydrazide.

[0838] Example 320

[0839] (R)-3-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-butyric acid hydrazide

[0840] Step 1: (R)-3-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-butyric acid methyl ester: To a solution of (R)-2-methylsuccinic acid 4-methyl ester (2.2 g, 15 mmol) and triethylamine (4.54 g, 45 mmol) in THF (30 ml), isobutylchloroformate (2.16 g, 15.8 mmol) was added dropwise at 0 °C. After being stirred for 30 min, the 3-chloro-N-hydroxy-benzamidine (2.56 g, 15 mmol) was added. The reaction mixture was stirred at room temperature for another 30 min and then heated to 135 °C with DMF for 45 min. The reaction mixture was diluted with ethyl acetate and washed with water and brine. The organic layer was dried and concentrated to give 4.0 g (95 %) of (R)-3-[3-(3-chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-butyric acid methyl ester as pale-yellow oil. Step 2: (R)-3-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-butyric acid hydrazide: (R)-3-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-butyric acid hydrazide (430 mg, 77%) was obtained from (R)-3-[3-(3-chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-butyric acid methyl ester (461.4 mg, 2.0 mmol) reacted with hydrazine hydrate (2mL) in methanol (2 mL) at 65 °C for 1 h. 1H-NMR($CDCl_3$) d (ppm): 8.07 (s, 1H), 7.96 (d, 1H), 7.46 (m, 2H), 6.98 (w, 1H), 3.93 (w, 2H), 3.78 (m, 1H), 2.86 (dd, 1H), 2.55 (dd, 1H) and 1.59 (d, 3H).

[0841] The following compounds were prepared analogously to Example 320:

Example No.	Name
321	3-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-3-methyl-butyric acid hydrazide

[0842] Example 322

[0843] **3-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethyl]-piperidin-2-one**

[0844] 1.33 ml (3.32 mmol) n-BuLi (2.5 M in hexanes) was added dropwise to a solution of 157 mg (1.58 mmol) d-valerolactone in 5,3 ml THF at 0 °C. After stirring

for 2 h at 0 °C, 400 mg (1.58 mmol) 3-chloromethyl-5-[3-chloro-phenyl)-[1,2,4]oxadiazole was added in one portion and stirring was continued for 3 h. NH_4Cl(sat) was added to quench the reaction and the mixture was extracted twice with CH_2Cl_2. The combined organic phases were dried and concentrated. Flashchromatography (SiO_2, Heptane/EtOAc 1:8) afforded 113 mg (25%) of a yellow-white solid. 1H NMR ($CDCl_3$):d ppm 1.80 (m, 1 H) 1.89 (m, 1 H) 2.00 (m, 1 H) 2.91 (m, 1 H) 2.98 (m, 1 H) 3.35 (m, 1 H) 3.52 (m, 1 H) 5.83 (s, 1 H) 7.46 (t, 1 H) 7.55 (d, J=8.08 Hz, 1 H) 8.00 (d, 1 H) 8.11 (s, 1 H).

[0845] The following compounds were prepared analogously to Example 322:

Example No.	Name
323	3-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethyl]-piperidin-2-one

[0846] Example 324

[0847] 3-Chloromethyl-5-(5-chloro-thiophen-3-yl)-[1,2,4]oxadiazole and 1-[5-(5-Chloro-thiophen-3-yl)-[1,2,4]oxadiazol-3-ylmethoxy]-1H-benzotriazole

[0848] A solution of 2-chloro-N-hydroxy-acetamidine (781 mg, 7.2 mmol), 5-chloro-thiophene-3-carboxylic acid (1.4 g), HBTU (3.55 g) and DIPEA (1.3 g) in DMF (20 ml) was stirred at ambient temperature for 1 h before heated at 120 °C for 4 h under argon. Removal of the solvent in vacuo followed by silica gel chromatography of the obtained residue using 0-20% EtOAc in n-heptane yielded 38.5 mg of the faster eluting 3-chloromethyl-5-(5-chloro-thiophen-3-yl)-[1,2,4]oxadiazole as a syrup, followed by 65 mg of the slower eluting 1-[5-(5-chloro-thiophen-3-yl)-[1,2,4]oxadiazol-3-ylmethoxy]-1H-benzotriazole as a white solid. 3-Chloromethyl-5-(5-chloro-thiophen-3-yl)-[1,2,4]oxadiazole: 1H NMR ($CDCl_3$) d (ppm): 8.01 (d, 1H), 7.50 (d, 1H), 4.63 (s, 2H). 1-[5-(5-Chloro-thiophen-3-yl)-[1,2,4]oxadiazol-3-ylmethoxy]-1H-benzotriazole: 1H NMR ($CDCl_3$) d (ppm): 7.97 (m, 2H), 7.52 (dt, 1H), 7.44 (m, 2H), 7.34 (m, 1H), 5.70 (s, 2H).

[0849] Example 325

[0850] **(4-Methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-acetonitrile**

[0851] 4-Methyl-5-thiophene-3-yl-4H-[1,2,4]triazole-3-thiol (197 mg, 1.0 mmol), chloroacetonitile (95 ml, 1.5 mmol), sodium carbonate (424 mg, 4 mmol) and potassium iodide (332mg, 2.0 mmol) were stirred together at 100 °C for 3 h with an additional addition of chloroacetonitrile (60ml, 0.5 mmol) after 2 h. The reaction was cooled, diluted with ethyl acetate and washed with water. The organic solution was dried, filtered and evaporated. Silica gel chromatography (dichloromethane:methanol 19:1) yielded 150 mg of the desired compound.

[0852] Example 326

[0853] 2-(4-Methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-propionic acid

[0854] (R)-2-chloro-propionic acid (500 mg, 4.6 mmol), 4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazole-3-thiol (1.09 g, 5.58 mmol) and potassium carbonate (1.94 g, 14.03 mmol) were dissolved in acetonitrile (15 ml) at room temperature. Reaction proceeded for 2.5 h and was partitioned between ethyl acetate (350 ml) and water 3 times, washed with 1 M HCl, once with saturated brine, dried over anhydrous sodium sulphate, filtered and concentrated in vacuo. Reaction was not completed at this stage and the crude was stirred in DMF (10 ml) overnight. Extraction was repeated and purification was performed by SPE (solid phase extraction) chromatography on silica gel using 300 ml ethyl acetate, 100 ml 1%, and 100 ml 3% formic acid in ethyl acetate, yielding title compound (150.7 mg, 12%) 1H-NMR ($CDCl_3$), d (ppm): 7.52 (dd, 2H), 7.19 (m, 1H), 4.21 (q, 1H), 3.78 (s, 3H), 1.64 (d, 3H).

[0855] The following compounds were prepared analogously to Example 326:

Example No.	**Name**
327	2-(4-Methyl-5-pyridin-3-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-propionic acid

[0856] Example 328

[0857] 3-(3-Chloro-phenyl)-5-(4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole

[0858] The title compound (2.08 g, 81.5 %) was obtained form 5-chloromethyl-3-(3-chloro-phenyl)-[1,2,4]oxadiazole (1.9 g, 8.29 mmol) reacted with 4-methyl-4H-[1,2,4]triazole-3-thiol (1.0 g, 8.71 mmol) and K_2CO_3 (4.58 g, 33.2 mmol) in DMF (19 ml) at room temperature overnight. 1H-NMR($CDCl_3$) d (ppm): 8.21 (s, 1H), 8.05 (s, 1H), 7.94 (d, 1H), 7.49(d, 1H), 7.43 (t, 1H), 4.69 (s, 2H) and 3.64(s, 3H).

[0859] Example 329

[0860] {3-[3-(4-Methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl-phenyl}-carbamic acid tert-butyl ester

[0861] The title compound was prepared from 4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazole-3-thiol (53 mg, 0.27 mmol), 3-(3-chloromethyl-[1,2,4]oxadiazol-5-yl)-phenyl]-carbamic acid tert-butyl ester (75 mg, 0.24 mmol), and potassium carbonate (101 mg, 0.73 mmol) in acetonitrile (2.5 ml). The product was purified by SPE (flash) chromatography using 65% ethyl acetate in hexane (88.0mg, 79%, white solid) . 1H NMR (CDCl$_3$) d (ppm): 8.06 (s, 1H), 7.73 (d, 1H), 7.66 (d, 1H), 7.51 (t, 2H), 7.42 (t, 1H), 7.18 (m, 1H), 6.68 (s, 1H), 4.51 (s, 2H), 3.73 (s, 3H), 1.53 (s, 9H).

[0862] The following compounds were prepared analogously to Example 41:

Example No.	Name	1H NMR	MS
330	4-(4-Cyclopropyl-5-{1-[5-(2,5-difluoro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4H-[1,2,4]triazol-3-yl)-pyridine	8.88 (d, 2H), 7.81 (m, 1H), 7.75 (m, 2H), 7.22 (m, 2H), 5.42 (q, 1H), 3.22 (m, 1H), 1.98 (d, 3H), 1.17 (m, 2H), 0.79 (m, 2H)	
331	4-(5-{1-[5-(3-Methoxy-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine	8.69 (m, 2H), 7.6 (m, 1H), 7.52 (m, 3H), 7.35 (t, 1H), 7.04 (m, 1H), 4.93 (q, 1H), 3.78 (t, 3H), 3.55 (s, 3H), 1.86 (d, 3H)	

332	4-{4-Methyl-5-[1-(5-m-tolyl-[1,2,4]oxadiazol-3-yl)-ethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine	8.71 (m, 2H), 7.82 (m, 2H), 7.53 (m, 2H), 7.32 (m, 2H), 4.94 (q, 1H), 3.54 (s, 3H), 2.33 (s, 3H), 1.87 (d, 3H)	
333	5-(4-Methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-o-tolyl-[1,2,4]oxadiazole	2.58 (s, 3 H) 3.70 (s, 3 H) 4.65 (s, 2 H) 7.17 (s, 1 H) 7.29 (s, 2 H) 7.36 (s, 1 H) 7.46 (s, 1 H) 7.51 (s, 1 H) 7.90 (s, 1 H)	370.0
334	5-(3-Chloro-phenyl)-3-(4-cyclopropyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	0.87 (m, 2 H) 1.18 (m, 2 H) 3.47 (ddd, J=6.95, 3.41, 3.28 Hz, 1 H) 4.70 (s, 2 H) 7.23 (m, 1 H) 7.67 (m, 2 H) 7.77 (m, 2 H) 8.04 (d, 2 H)	415.9
335	2-{3-[5-(2-Fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-5-thiophen-2-yl-[1,2,4]triazol-4-yl}-ethanol	2.36 (s, 3 H) 4.03 (t, 2 H) 4.30 (t, 2 H) 4.57 (s, 2 H) 7.11 (m, 2 H) 7.35 (s, 1 H) 7.47 (d, 1 H) 7.64 (d, 1 H) 7.81 (d, 1 H)	417.9
336	4-{4-Ethyl-5-[5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyrimidine	1.38 (t, 3 H) 2.34 (s, 3 H) 4.66 (m, 4 H) 7.19 (m, 1 H) 7.47 (m, 1 H) 7.83 (d,1 H) 8.23 (d, 1 H) 8.94 (d, 1 H) 9.28 (s, 1 H)	398.0

337	3-(4-Ethyl-5-furan-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazole	1.34 (t, 3 H) 2.37 (s, 3 H) 4.06 (q, 2 H) 4.61 (s, 2 H) 6.82 (s, 1 H) 7.12 (m, 1 H) 7.36 (ddd, 1 H) 7.55 (s, 1 H) 7.85 (d, 2 H).	386.0
338	{3-[5-(2-Fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-5-thiophen-2-yl-[1,2,4]triazol-4-yl}-acetic acid methyl ester	2.36 (s, 3 H) 3.70 (s, 3 H) 4.46 (s, 2 H) 5.10 (s, 2 H) 7.21 (m, 2 H) 7.47 (m, 2 H) 7.73 (d, 1 H) 7.86 (m, 1 H)	445.9
339	5-(2-Fluoro-5-methyl-phenyl)-3-[5-furan-2-yl-4-(2-methoxy-ethyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole	2.26 (s, 3 H) 3.16 (s, 3 H) 3.57 (t, 2 H) 4.42 (t, 2 H) 4.44 (s, 2 H) 6.60 (s, 1 H) 7.10 (m, 2 H) 7.37 (m, 1 H) 7.70 (s, 1 H) 7.73 (d,1 H)	416.0
340	3-(4-Cyclopropyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazole	0.87 (m, 2 H) 1.14 (m, 2 H) 2.35 (s, 3 H) 3.39 (dt, 1 H) 4.71 (s, 2 H) 6.72 (s, 1 H) 7.09 (d, 1 H) 7.39 (m, 1 H) 7.56 (m, 1 H) 7.87 (d, 1 H) 7.93 (s, 1 H)	398.0
341	3-(5-Chloro-2-fluoro-phenyl)-5-(4-cyclopropylmethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	0.32 (m, 2 H) 0.56 (m, 2 H) 1.14 (d, 1 H) 4.00 (d, 2 H) 4.76 (s, 2 H) 7.16 (ddd, 2 H) 7.43 (m, 1 H) 7.50 (t, 2 H) 7.99 (dd, 1 H)	448.1

342	4-{5-[3-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyrimidine	1.40 (t, 3 H) 4.63 (q, 2 H) 4.72 (s, 2 H) 7.20 (m, 1 H) 7.53 (m, 1 H) 8.06 (dd, 1 H) 8.29 (d, 1 H) 8.86 (d, 1 H) 9.26 (s, 1 H).	417.8
343	3-(5-Cyclopentyl-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole	1.29 (t, 3 H) 1.66 (m, 3 H) 1.87 (m, 2 H) 2.02 (m, 3 H) 2.42 (s, 3 H) 3.01 (s, 2 H) 3.90 (d, 2 H) 4.52 (s, 2 H) 7.39 (d, 2 H) 7.90 (d, 2 H)	370.2
344	3-(3-Chloro-phenyl)-5-{4-ethyl-5-[2-(4-methoxy-phenyl)-ethyl]-4H-[1,2,4]triazol-3-ylsulfanylmethyl}-[1,2,4]oxadiazole	1.18 (t, 3 H) 2.95 (t, 2 H) 3.09 (t, 2 H) 3.72 (q, 2 H) 3.76 (s, 3 H) 4.66 (s, 2 H) 6.81 (d, 2 H) 7.09 (d, 2 H) 7.40 (t, 1 H) 7.47 (m, 1 H) 7.92 (d, 1 H) 8.03 (s, 1 H)	456.1
345	5-(3-Chloro-phenyl)-3-(4-ethyl-5-p-tolyloxymethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	1.23 (t, 3 H) 2.22 (s, 3 H) 4.02 (d, 2 H) 4.60 (s, 2 H) 5.22 (s, 2 H) 6.92 (d, 2 H) 7.09 (d, 2 H) 7.65 (t, 1 H) 7.79 (d, 1 H) 8.04 (m, 2 H)	442.1
346	5-(3-Chloro-phenyl)-3-[4-(2-methoxy-ethyl)-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole	3.14 (s, 3 H) 3.57 (t, 2 H) 4.30 (t, 2 H) 4.58 (s, 2 H) 7.23 (m, 1 H) 7.64 (m, 2 H) 7.78 (m, 2 H) 8.03 (d, 2 H)	433.9

347	3-(5-Chloro-2-fluoro-phenyl)-5-(4-ethyl-5-methoxymethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	7.98 (m, 1H), 7.43 (m, 1H), 7.16 (apparent t, 1H), 4.73 (s, 2H), 4.62 (s, 2H), 4.01 (q, 2H), 3.33 (s, 3H), 1.34 (t, 3H).	384.9
348	5-(5-Chloro-2-fluoro-phenyl)-3-(4-ethyl-5-methoxymethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	8.05 (m, 1H), 7.53 (m, 1H), 7.21 (apparent t, 1H); 4.62 (s, 2H), 4.61 (s, 2H), 4.02 (q, 2H), 3.34 (s, 3H), 1.32 (t, 3H).	384.9
349	5-(3-Chloro-phenyl)-3-(4-ethyl-5-methoxymethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	8.07 (apparent s, 1H), 7.97 (m, 1H), 7.55 (m, 1H), 7.45 (apparent t, 1H), 4.62 (s, 2H), 4.59 (s, 2H), 4.01 (q, 2H), 3.34 (s, 3H), 1.32 (t, 3H).	366.9
350	3-(3-Chloro-phenyl)-5-(4-ethyl-5-methoxymethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	8.02 (m, 1H), 7.92 (m, 1H), 7.46 (m, 1H), 7.39 (apparent t, 1H), 4.71 (s, 2H), 4.62 (s, 2H), 4.01 (q, 2H), 3.34 (s, 3H), 1.34 (t, 3H).	366.9
351	4-(5-{1-[3-(3-Chloro-phenyl)-isoxazol-5-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine	1.82 (d, 3 H), 3.46 (s, 3 H), 4.93 (q, 1 H), 6.33 (s, 1 H), 7.23-7.31 (m, 2 H), 7.44 (d, 2 H), 7.49 (m, 1 H), 7.61 (s, 1 H), 8.63 (d, 2 H).	399.1

352	3-(4-Allyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-chloro-phenyl)-[1,2,4]oxadiazole	4.6 (s, 2 H), 4.8 (d, 2 H), 5.0 (d, 1 H), 5.2 (d, 1 H), 5.9 (m, 1 H), 6.5 (m, 1 H), 7.1 (d, 1 H), 7.4 (t, 1 H), 7.5 (m, 2 H), 8.0 (d, 1 H), 8.1 (s, 1 H)	399.95
353	3-(4-Allyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-3-yl-[1,2,4]oxadiazole	4.5 (s, 2 H) 4.8 (d, 2 H) 5.0 (d, 1 H) 5.2 (d, 1 H) 5.9 (m, 1 H) 6.5 (m, 1 H) 7.0 (d, 1 H) 7.4 (m, 1 H) 7.5 (s, 1 H) 7.6 (d, 1 H) 8.2 (m, 1 H)	371.98
354	5-(4-Allyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-furan-2-yl-[1,2,4]oxadiazole	4.7 (s, 2 H) 4.8 (m, 2 H) 5.0 (d, 1 H) 5.2 (d, 1 H) 5.9 (m, 1 H) 6.5 (dt, 2 H) 7.1 (dd, 2 H) 7.6 (dd, 2 H)	356.01
355	5-(3-Chloro-phenyl)-3-[4-ethyl-5-(4-methoxy-phenoxymethyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole	1.4 (t, 3 H) 3.7 (s, 3 H) 4.1 (q, 2 H) 4.6 (s, 2 H) 5.2 (s, 2 H) 6.8 (d, 2 H) 6.9 (d, 2 H) 7.4 (t, 1 H) 7.6 (d, 1 H) 8.0 (d, 1 H) 8.1 (s, 1 H)	457.91
356	3-(3-Chloro-phenyl)-5-[4-ethyl-5-(4-methoxy-phenoxymethyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole	1.4 (t, 3 H) 3.7 (s, 3 H) 4.1 (q, 2 H) 4.8 (s, 2 H) 5.2 (s, 2 H) 6.8 (d, 2 H) 6.9 (d, 2 H) 7.4 (t, 1 H) 7.5 (m, 1 H) 7.9 (d, 1 H) 8.0 (s, 1 H)	457.97

357	{5-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-methanol	1.4 (t, 3 H) 4.2 (d, 2 H) 4.7 (s, 2 H) 4.9 (s, 2 H) 7.4 (t, 1 H) 7.5 (m, 1 H) 7.9 (d, 1 H) 8.0 (s, 1 H)	352.09
358	3-(3-Chloro-phenyl)-5-[4-ethyl-5-(2-methoxy-ethyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole	1.3 (t, 3 H) 3.0 (t, 2 H) 3.3 (s, 3 H) 3.8 (t, 2 H) 3.9 (q, 2 H) 4.7 (s, 2 H) 7.4 (t, 1 H) 7.5 (ddd, 1 H) 7.9 (dt, 1 H) 8.0 (t, 1 H)	380.12
359	3-(3-Chloro-phenyl)-5-(4-ethyl-5-methylsulfanylmethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	1.4 (t, 3 H) 2.1 (s, 3 H) 3.8 (s, 2 H) 4.0 (q, 2 H) 4.7 (s, 2 H) 7.4 (t, 1 H) 7.5 (ddd, 1 H) 7.9 (dt, 1 H) 8.0 (t, 1 H)	382.07
360	3-(3-Chloro-phenyl)-5-(5-ethoxymethyl-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	.2 (t, 3 H) 1.3 (t, 3 H) 3.5 (q, 2 H) 4.0 (q, 2 H) 4.7 (s, 2 H) 4.7 (s, 2 H) 7.4 (t, 1 H) 7.5 (ddd, 1 H) 7.9 (dt, 1 H) 8.0 (t, 1 H)	379.13
361	5-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazole-3-carboxylic acid methyl ester		

362	2-(5-Chloro-2-fluoro-phenyl)-5-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazole	1.4 (t 3 H) 4.2 (q, 2 H) 4.7 (s, 2 H) 6.6 (dd, 1 H) 7.1 (d, 1 H) 7.2 (m, 1 H) 7.5 (ddd, 1 H) 7.6 (d, 1 H) 8.0 (dd, 1 H)	406.07
363	2-(3-Chloro-phenyl)-5-(4-cyclopropyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazole	0.9 (m, 2 H) 1.2 (m, 2 H) 3.2 (m, 1 H) 4.8 (s, 2 H) 6.6 (m, 1 H) 7.0 (d, 1 H) 7.4 (t, 1 H) 7.5 (m, 1 H) 7.6 (m, 1 H) 7.9 (m, 1 H) 8.0 (m, 1 H)	399.86
364	5-(3-Chloro-phenyl)-3-{1-[4-ethyl-5-(tetrahydro-furan-2-yl)-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,2,4]oxadiazole	1.3 (t, 3 H) 1.9 (d, 3 H) 2.0 (m, 1 H) 2.1 (m, 1 H) 2.3 (m, 1 H) 2.8 (m, 1 H) 3.8 (m, 2 H) 4.0 (m, 1 H) 4.1 (m, 1 H) 5.0 (m, 1 H) 5.1 (m, 1 H) 7.4 (t, 1 H) 7.6 (m, 1 H) 8.0 (m, 1 H) 8.1 (s, 1 H)	406.04
365	4-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyridazine	1.4 (t, 3 H) 1.9 (d, 3 H) 4.1 (m, 2 H) 5.2 (q, 1 H) 7.4 (t, 1 H) 7.5 (m, 1 H) 7.8 (m, 1 H) 8.0 (m, 1 H) 8.1 (m, 1 H) 9.4 (m, 1 H) 9.5 (s, 1 H)	414.12

366	4-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-ylmethyl)-pyridine	1.0 (t, 3 H) 1.9 (d, 3 H) 3.7 (m, 2 H) 4.2 (m, 2 H) 5.0 (q, 1 H) 7.1 (m, 2 H) 7.4 (t, 1 H) 7.5 (m, 1 H) 7.9 (d, 1 H) 8.1 (s, 1 H) 8.5 (m, 2 H)	427.06
367	5-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyridin-2-ol	1.3 (t, 3 H) 1.9 (d, 3 H) 3.9 (m, 2 H) 5.1 (q, 1 H) 6.7 (d, 1 H) 7.5 (t, 1 H) 7.6 (m, 1 H) 7.7 (m, 1 H) 7.7 (s, 1 H) 8.0 (d, 1 H) 8.1 (s, 1 H) 13.1 (s, 1 H)	429.1
368	4-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-phenol	1.2 (t, 3 H) 1.9 (d, 3 H) 3.9 (q, 2 H) 5.1 (q, 1 H) 6.9 (d, 2 H) 7.3 (d, 2 H) 7.4 (t, 1 H) 7.5 (m, 1 H) 7.9 (m, 1 H) 8.1 (m, 1 H) 10.2 (s, 1 H)	428.08
369	5-(3-Chloro-phenyl)-3-[5-(4-methoxy-phenoxymethyl)-4-(tetrahydro-furan-2-ylmethyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole	1.54 (m, 1 H) 1.86 (m, 2 H) 2.02 (m, 1 H) 3.71 (m, 4 H) 3.79 (m, 1 H) 4.13 (m, 3 H) 4.60 (m, 2 H) 5.30 (s, 2 H) 6.82 (m, 2 H) 6.92 (m, 2 H) 7.44 (t, 1 H) 7.55 (d, 1 H) 7.95 (d, 1 H) 8.07 (s, 1 H)	

370	5-(3-Chloro-phenyl)-3-[4-cyclopropyl-5-(4-methoxy-phenoxymethyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole	1.14 (m, 4 H) 3.10 (s, 1 H) 3.75 (s, 3 H) 4.70 (s, 2 H) 5.21 (s, 2 H) 6.82 (d, 2 H) 6.95 (d, 2 H) 7.45 (t, 1 H) 7.56 (m, 1 H) 7.99 (d, 1 H) 8.10 (s, 1 H)	
371	5-(5-Chloro-2-fluoro-phenyl)-3-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	1.38 (t, 3 H) 4.27 (q, 2 H) 4.64 (s, 2 H) 6.58 (m, 1 H) 7.21 (m, 2 H) 7.53 (m, 1 H) 7.59 (m, 1 H) 8.06 (m, 1 H)	
372	3-(4-Ethyl-5-methoxymethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole	1.29 (t, 3 H) 2.40 (s, 3 H) 3.31 (s, 3 H) 3.99 (m, 2 H) 4.56 (s, 2 H) 4.60 (s, 2 H) 7.37 (m, 2 H) 7.87 (m, 2 H)	346
373	3-[4-Ethyl-5-(tetrahydro-furan-2-yl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-5-m-tolyl-[1,2,4]oxadiazole	1.30 (t, 3 H) 1.97 (m, 1 H) 2.10 (m, 1 H) 2.24 (m, 1 H) 2.39 (s, 3 H) 2.80 (m, 1 H) 3.79 (m, 1 H) 3.86 (m, 1 H) 3.99 (m, 1 H) 4.08 (m, 1 H) 4.54 (m, 2 H) 4.98 (m, 1 H) 7.36 (m, 2 H) 7.86 (m, 1 H) 7.88 (s, 1 H)	372

374	2-(3-Chloro-phenyl)-5-{1-[4-ethyl-5-(4-methoxy-phenyl)-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,3,4]oxadiazole	1.18 (m, 3 H) 1.95 (d, 3 H) 3.81 (s, 3 H) 3.90 (q, 2 H) 5.15 (q, 1 H) 6.94 (m, 2 H) 7.35 (m, 1 H) 7.45 (m, 3 H) 7.81 (m, 1 H) 7.92 (m, 1 H)	
375	4-{5-[3-(2,5-Difluoro-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyrimidine	1.43 (t, 3 H), 4.64 (q, 2 H), 4.87 (s, 2 H), 7.18 (m, 2 H), 7.72 (m, 1 H), 8.29 (dd, 1 H), 8.89 (d, 1 H), 9.30 (d, 1 H)	402.1
376	4-{5-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyrimidine	4.12 (s, 3 H), 4.64 (s, 2 H), 7.21 (t, 1 H), 7.57 (m, 1 H), 8.06 (dd, 1 H), 8.28 (dd, 1 H), 8.92 (d, 1 H), 9.30 (d, 1 H)	404.1
377	3-(3-Chloro-phenyl)-5-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	8.03 (s, 1H), 7.92 (d, 1H), 7.53 (d, 1H), 7.48 (m, 2H), 7.40 (t, 1H), 7.18 (t, 1H), 4.87 (s, 2H), 3.72 (s, 3H).	390.96
378	5-(3-Methylsulfanyl-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	7.92 (s, 1H), 7.84 (d, 1H), 7.53 (m, 2H), 7.43 (m, 2H), 7.18 (m, 1H), 4.53 (s, 2H), 3.73 (s, 3H), 2.52 (s, 3H).	
379	2-[5-(3-Methylsulfanyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1H-benzoimidazole		

380	5-(2,5-Dimethyl-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	7.87 (s, 1H), 7.49 (m, 2H), 7.22 (m, 3H), 4.56 (d, 2H), 3.74 (s, 3H), 2.61 (s, 3H), 2.37 (s, 3H).	
381	5-(2-Fluoro-5-methyl-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	7.83 (dd, 1H), 7.49 (m, 2H), 7.35 (m, 1H), 7.16 (m, 2H), 4.53 (s, 2H), 3.73 (s, 3H), 2.35 (s, 3H).	388.10
382	5-(3-Cyclopropyl-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	7.87 (d, 1H), 7.79 (s, 1H), 7.51 (m, 2H), 7.40 (t, 1H), 7.30 (m, 1H), 7.20 (m, 1H), 4.53 (s, 2H), 3.73 (s, 3H), 1.96 (m, 1H), 1.04 (m, 2H), 0.77 (m, 2H).	
383	4-{5-[2-(3-Chloro-phenyl)-oxazol-4-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.80 (d, 2H), 8.02 (dd, 1H), 7.88 (dd, 1H), 7.80 (s, 1H), 7.60 (d, 2H), 7.42 (m, 2H), 4.51 (s, 2H), 3.64 (s, 3H).	
384	4-[4-Methyl-5-(5-thiophen-2-yl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine	8.82 (bs, 2H), 7.90 (m, 1H), 7.66 (m, 3H), 7.22 (m, 1H), 4.58 (s, 2H), 3.73 (s, 3H).	

385	4-{4-Methyl-5-[5-(3-methylsulfanyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine	8.81 (m, 2H), 7.95 (s, 1H), 7.86 (m, 1H), 7.64 (m, 2H), 7.45 (m, 2H), 4.63 (s, 2H), 3.72 (s, 3H), 2.55 (3H).	
386	4-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.83 (d, 2H), 8.11 (s, 1H), 8.00 (d, 1H), 7.64 (m, 2H), 7.60 (m, 1H), 7.49 (t, 1H), 4.64 (s, 2H), 3.73 (s, 3H).	
387	2-Methyl-4-[3-(4-methyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine	8.82 (d, 2H), 8.74 (d, 1H), 7.82 (s, 1H), 7.76 (d, 1H), 7.64 (d, 2H), 4.68 (s, 2H), 3.74 (s, 3H), 2.68 (s, 3H).	
388	1-{3-[3-(4-Methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-phenyl}-ethanone	8.67 (s, 1H), 8.29 (d, 1H) 8.20 (d, 1H), 7.68 (t, 1H), 7.52 (m, 2H), 7.20 (m, 1H), 4.58 (s, 2H), 3.76 (s, 3H), 2.68 (s, 3H).	
389	4-{5-[5-(2-Fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.81 (dd, 2H), 7.86 (d, 1H), 7.64 (m, 2H), 7.39 (m, 1H), 7.14 (dd, 1H), 4.63 (s, 2H), 3.73 (s, 3H), 2.39 (s, 3H).	383.09

390	2-Methyl-4-[4-methyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine	8.68 (dd, 1H), 7.92 (m, 2H), 7.52 (bs, 1H), 7.4 (m, 3H), 4.61 (s, 2H), 3.7 (s, 3H), 2.67 (s, 3H), 2.44 (s, 3913H).	
391	3-[5-(3-Chloro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazole	7.76 (s, 1H), 7.68 (m, 1H), 7.54 (m, 1H), 7.48 (m, 1H), 7.40 (m, 2H), 7.20 (m, 1H), 6.76 (s, 1H), 4.56 (s, 2H), 3.70 (s, 3H).	
392	4-{5-[5-(3-Chloro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.82 (m, 2H), 7.76 (m, 1H), 7.65 (m, 3H), 7.41 (m, 2H), 6.77 (s, 1H), 4.61 (s, 2H), 3.69 (s, 3H).	
393	3-(4-Butyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-chloro-phenyl)-[1,2,4]oxadiazole	8.07 (s, 1H), 7.95 (dd, 1H), 7.48 (m, 4H), 7.17 (dd, 1H), 4.59 (s, 2H), 4.05 (t, 2H), 1.67 (m, 2H), 1.30 (m, 2H), 0.88 (t, 3H).	
394	5-(3-Chloro-phenyl)-3-[4-(3-methoxy-propyl)-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole	8.01 (d, 1H), 7.91 (dd, 1H), 7.48 (m, 4H), 7.12 (m, 1H), 4.51 (s, 2H), 4.17 (t, 2H), 3.34 (t, 2H), 3.18 (s, 3H), 1.90 (m, 2H).	

395	3-(4-Benzyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-chloro-phenyl)-[1,2,4]oxadiazole	8.09 (s, 1H), 7.97 (dd, 1H), 7.57 (m, 1H), 7.47 (m, 2H), 7.24 (m, 4H), 7.06 (m, 3H), 5.37 (s, 2H), 4.57 (s, 2H).	
396	5-(3-Chloro-phenyl)-3-(4-furan-2-ylmethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	8.10 (d, 1H), 8.03 (dd, 1H), 7.55 (m, 4H), 7.38 (s, 1H), 7.20 (dd, 1H), 6.32 (m, 2H), 5.30 (s, 2H), 4.60 (s, 2H).	457.02
397	3-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.93 (m, 1H), 8.78 (m, 1H), 8.03 (m, 3H), 7.59 (m, 1H), 7.51 (m, 2H), 4.63 (s, 2H), 3.69 (s, 3H).	
398	5-(3-Chloro-phenyl)-3-(4-methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	8.11 (m, 1H), 8.05 (m, 1H), 7.74 (m, 1H), 7.59 (m, 1H), 7.51 (m, 3H), 4.57 (s, 2H), 3.71 (s, 3H).	
399	4-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-2-methyl-pyridine	8.69 (d, 1H), 8.10 (s, 1H), 8.00 (m, 1H), 7.49 (m, 4H), 4.63 (s, 2H), 3.71 (s, 3H), 2.67 (s, 3H).	
400	5-(5-Chloro-2-fluoro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	8.08 (m, 1H), 7.51 (m, 1H) 7.21 (m, 1H), 4.59 (s, 2H), 3.77 (s, 3H).	409.00

401	4-{5-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.82 (d, 2H), 8.08 (m, 1H) 8.29 (d, 1H), 7.64 (d, 2H), 7.56 (m, 1H), 7.24 (t, 1H), 4.66 (s, 2H), 3.75 (s, 3H).	404.07
402	3-{5-[5-(2-Fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.92 (s, 1H), 8.76 (d, 1H), 8.07 (d, 1H), 7.87 (d, 1H), 7.36 (m, 3H), 4.59 (s, 2H), 3.69 (s, 3H), 2.39 (s, 3H).	
403	5-(3-Chloro-phenyl)-3-(5-thiophen-2-yl-4-thiophen-2-ylmethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	(CD3OD as solvent): 8.05 (m, 1H), 8.00 (dd, 1H), 7.75 (dd, 1H), 7.58 (m, 1H), 7.54 (m, 1H), 7.53 (m, 1H), 7.26 (m, 1H), 7.22 (m, 1H), 6.86 (m, 2H), 5.63 (s, 2H), 4.51 (s, 2H).	
404	5-(3-Chloro-phenyl)-3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	(CD3OD as solvent):8.08 (m, 1H), 8.07 (dd, 1H), 7.75 (m, 1H), 7.67 (m, 1H), 7.60 (m, 2H), 7.28 (dd, 1H), 4.57 (s, 2H), 4.27 (m, 2H), 1.29 (m, 3H).	405.10
405	3-{5-[3-(2-Fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.90 (m, 1H), 8.77 (dd, 1H), 8.03 (m, 1H), 7.78 (m, 1H), 7.48 (m, 1H), 7.28 (m, 1H), 7.12 (m, 1H), 4.73 (s, 2H), 3.68 (s, 3H), 2.36 (s, 3H).	

406	4-{5-[3-(2-Fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.81 (m, 2H), 7.77 (m, 1H), 7.62 (m, 2H), 7.31 (m, 1H), 7.11 (dd, 1H), 4.75 (s, 2H), 3.72 (s, 3H), 2.37 (s, 3H).	
407	4-{5-[5-(5-Bromo-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.82 (m, 2H), 8.23 (m, 1H), 7.71 (m, 2H), 7.65 (m, 1H), 7.18 (d, 1H), 4.66 (s, 2H), 3.75 (s, 3H).	448.02
408	3-{5-[5-(5-Bromo-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.92 (m, 1H), 8.76 (m, 1H), 8.22 (m, 1H), 8.05 (m, 1H), 7.50 (m, 1H), 7.48 (m, 1H), 7.17 (dd, 1H), 4.63 (s, 2H), 3.70 (s, 3H).	
409	5-(5-Bromo-2-fluoro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	8.23 (dd, 1H), 7.70 (m, 1H), 7.52 (m, 2H), 7.19 (m, 2H), 4.49 (s, 2H), 3.77 (s, 3H).	452.90
410	5-(4-Methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-phenyl-[1,2,4]oxadiazole	8.06 (d, 2H) 7.34 (d, 1H), 7.51 (m, 5H), 4.68 (s, 2H), 3.68 (s, 3H).	
411	3-{5-[5-(3-Fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.92 (s, 1H), 8.78 (d, 1H) 8.05 (d, 1H), 7.93 (d, 1H), 7.91 (d, 1H), 7.50 (m, 2H), 7.28 (t, 1H), 4.64 (s, 2H), 3.70 (s, 3H).	

412	4-{5-[5-(3-Fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.82 (d, 2H), 7.93 (d, 1H) 7.90 (d, 1H), 7.64 (d, 2H), 7.52 (m, 1H), 7.33 (m, 1H), 4.64 (s, 2H), 3.73 (s, 3H).	
413	5-(3-Fluoro-phenyl)-3-(4-methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	7.90 (d, 1H) 7.82 (d, 1H), 7.74 (d, 1H), 7.51 (m, 3H), 4.58 (s, 2H), 3.71 (s, 3H).	
414	3-[4-Methyl-5-(5-thiophen-3-yl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine	8.91 (s, 1H), 8.78 (d, 1H) 8.23 (d, 1H), 8.04 (d, 1H), 7.66 (d, 1H), 7.49 (m, 2H), 4.60 (s, 2H), 3.69 (s, 3H).	
415	3-(4-Methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-3-yl-[1,2,4]oxadiazole	8.22 (d, 1H) 7.74 (d, 1H), 7.63 (d, 1H), 7.49 (m, 3H), 4.54 (s, 2H), 3.70 (s, 3H).	
416	2-Chloro-4-[3-(4-methyl-5-pyridin-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine	8.92 (s, 1H), 8.78 (d, 1H) 8.65 (d, 1H), 8.04 (t, 2H), 7.89 (d, 1H), 7.51 (m, 1H), 4.69 (s, 2H), 3.71 (s, 3H).	
417	2-Chloro-4-[3-(4-methyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine	8.82 (d, 2H), 8.65 (d, 1H) 8.02 (s, 1H), 7.89 (d, 1H), 7.64 (d, 2H), 4.70 (s, 2H), 3.74 (s, 3H).	

418	2-Chloro-4-[3-(4-methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine	8.64 (d, 1H) 8.01 (s, 1H), 7.88 (d, 1H), 7.75 (d, 1H), 7.52 (m, 2H), 4.62 (s, 2H), 3.72 (s, 3H).	
419	4-[4-Methyl-5-(5-phenyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine	8.82 (d, 2H), 8.12 (d, 2H) 7.63 (m, 3H), 7.55 (m, 2H), 4.63 (s, 2H), 3.72 (s, 3H).	
420	3-(4-Methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-phenyl-[1,2,4]oxadiazole	8.11 (d, 2H) 7.74 (d, 1H), 7.57 (m, 1H), 7.52 (m, 4H), 4.56 (s, 2H), 3.70 (s, 3H).	
421	5-(5-Bromo-2-fluoro-phenyl)-3-(4-methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	(CD3OD as solvent):8.21 (m, 1H), 8.02 (m, 1H), 7.82 (m, 1H), 7.68 (m, 1H), 7.56 (m, 1H), 7.33 (t, 1H), 4.50 (s, 2H), 3.82 (s, 3H).	
422	3-[5-(3-Chloro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazole	(CD3OD as solvent): 7.84 (s, 1H), 7.75 (m, 2H), 7.60 (m, 1H) 7.50 (m, 2H), 7.27 (m, 1H), 6.92 (s, 1H), 4.51 (s, 2H), 4.23 (q, 2H), 1.33 (t, 3H).	404.05

423	2-Chloro-4-[3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine	8.64 (d, 1H), 8.01 (s, 1H) 7.98 (d, 1H), 7.54 (d, 1H), 7.50 (d, 1H), 7.20 (m, 1H), 4.61 (s, 2H), 3.76 (s, 3H).	392.00
424	4-{5-[3-(3-Fluoro-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.83 (d, 2H), 7.85 (d, 1H) 7.78 (d, 1H), 7.62 (d, 2H), 7.46 (m, 1H), 7.22 (m, 1H), 4.76 (s, 2H), 3.72 (s, 3H).	
425	3-(3-Fluoro-phenyl)-5-(4-methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	7.84 (d, 1H) 7.74 (m, 1H), 7.51 (m, 3H), 7.24 (m, 1H), 4.70 (s, 2H), 3.70 (s, 3H).	
426	3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole	(CD3OD as solvent):7.89 (m, 2H), 7.76 (m, 1H), 7.60 (m, 1H), 7.47 (m, 2H), 7.27 (m, 1H), 4.55 (s, 2H), 4.25 (q, 2H), 2.41 (s, 3H), 1.32 (s, 3H)	384.13
427	3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazole	(CD3OD as solvent):7.85 (m, 1H), 7.75 (m, 1H), 7.60 (m, 1H), 7.55 (m, 1H), 7.27 (m, 1H), 7.22 (m, 1H), 4.57 (s, 2H), 4.27 (q, 2H), 2.36 (s, 3H), 1.33 (s, 3H).	402.09

428	4-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-furan-2-ylmethyl-4H-[1,2,4]triazol-3-yl}-pyridine	(CD3OD as solvent):8.75 (m, 2H), 8.04 (m, 2H), 7.78 (m, 2H), 7.66 (m, 1H), 7.60 (m, 1H), 7.37 (m, 1H), 6.30 (m, 2H), 5.42 (s, 2H), 4.56 (s, 2H).	452.10
429	4-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.80 (m, 2H), 8.09 (m, 1H), 7.98 (m, 1H), 7.58 (m, 3H), 7.50 (dd, 1H), 4.69 (s, 2H), 4.12 (m, 2H), 1.36 (m, 3H).	
430	3-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine	(CD3OD as solvent):8.87 (s, 1H), 8.77 (d, 1H), 8.07 (m, 3H), 7.67 (m, 2H), 7.61 (dd, 1H), 4.62 (s, 2H), 4.13 (m, 2H), 1.26 (m, 3H).	400.12
431	5-(3-Chloro-phenyl)-3-(4-ethyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	(CD3OD as solvent):7.79 (m, 3H), 7.67 (m, 2H), 7.51 (m, 2H), 4.56 (s, 2H), 4.22 (q, 2H), 1.30 (t, 3H).	405.07
432	3-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-furan-2-ylmethyl-4H-[1,2,4]triazol-3-yl}-pyridine	(CD3OD as solvent):8.86 (s, 1H), 8.76 (d, 1H), 8.07 (m, 1H), 8.01 (m, 2H), 7.64 (m, 3H), 7.36 (s, 1H), 6.29 (s, 2H), 5.37 (s, 2H), 4.55 (s, 2H).	452.12

433	3-(4-Furan-2-ylmethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole	(CD3OD as solvent):7.87 (m, 2H), 7.73 (m, 1H), 7.63 (m, 1H), 7.45 (m, 3H), 7.25 (m, 1H), 6.31 (m, 2H), 5.42 (s, 2H), 4.49 (s, 2H), 2.40 (s, 3H).	436.16
434	5-(5-Fluoro-2-methyl-phenyl)-3-(4-furan-2-ylmethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	(CD3OD as solvent):7.75 (dd, 1H), 7.69 (m, 1H), 7.66 (m, 1H), 7.41 (m, 1H), 7.38 (m, 1H), 7.25 (m, 2H), 6.32 (s, 2H), 5.44 (s, 2H), 4.51 (s, 2H), 2.36 (s, 3H).	454.12
435	5-(3-Chloro-phenyl)-3-(4-furan-2-ylmethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	8.23 (s, 1H), 8.09 (m, 1H), 7.97 (m, 1H), 7.48 (m, 1H), 7.45 (m, 1H), 7.37 (s, 1H), 6.39 (m, 1H), 6.34 (m, 1H), 5.12 (s, 2H), 4.55 (s, 2H).	375.09
436	3-[3-(4-Methyl-5-pyridin-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzonitrile	8.92 (s, 1H), 8.78 (d, 1H) 8.43 (s, 1H), 8.35 (d, 1H), 8.05 (d, 1H), 7.91 (d, 1H), 7.72 (t, 1H), 7.52 (m, 1H), 4.67 (s, 2H), 3.71 (s, 3H).	376.20

437	3-[3-(4-Methyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzonitrile	8.82 (d, 2H), 8.43 (s, 1H) 8.35 (d, 1H), 7.90 (t, 1H), 7.64 (d, 2H), 4.68 (s, 2H), 3.74 (s, 3H).	376.10
438	3-[3-(4-Methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzonitrile	8.42 (s, 1H), 8.35 (d, 1H) 7.89 (d, 1H), 7.72 (m, 2H), 7.52 (s, 1H), 4.61 (s, 2H), 3.73 (s, 3H).	
439	5-(5-Chloro-2-fluoro-phenyl)-3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	8.08 (m, 1H), 7.54 (m, 2H), 7.48 (d, 1H), 7.20 (m, 2H), 4.69 (s, 2H), 4.18 (m, 2H), 1.39 (t, 3H).	423.12
440	2-Chloro-4-[3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine	8.64 (d, 1H), 8.02 (s, 1H), 7.89 (d, 1H), 7.53 (d, 1H), 7.48 (d, 1H), 7.20 (t, 1H), 4.69 (s, 2H), 4.17 (m, 2H), 1.40 (t, 3H).	406.00
441	3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-3-yl-[1,2,4]oxadiazole	8.23 (s, 1H), 7.66 (d, 1H), 7.53 (d, 1H), 7.48 (m, 2H), 7.19 (t, 1H), 4.63 (s, 2H), 4.17 (m, 2H), 1.40 (t, 3H).	376.10

442	3-(4-Ethyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole	7.93 (m, 2H), 7.71 (m, 1H), 7.49 (m, 2H), 7.42 (m, 2H), 4.63 (s, 2H), 4.10 (q, 2H), 2.43 (s, 3H), 1.36 (t, 3H).	384.10
443	4-[4-Ethyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine	8.80 (m, 2H), 7.91 (m, 2H), 7.60 (m, 2H), 7.41 (m, 2H), 4.68 (s, 2H), 4.09 (m, 2H), 2.43 (s, 3H), 1.29 (s, 3H).	379.20
444	3-[4-Ethyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine	(CD3OD as solvent):8.87 (s, 1H), 8.77 (d, 1H), 8.02 (m, 1H), 7.92 (m, 2H), 7.49 (m, 1H), 7.42 (m, 2H), 4.67 (s, 2H), 4.05 (q, 2H), 2.43 (s, 3H), 1.35 (t, 3H).	379.20
445	3-(4-Ethyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazole	7.88 (dd, 1H), 7.71 (m, 1H), 7.49 (m, 2H), 7.28 (m, 1H), 7.14 (dd, 1H), 4.66 (s, 2H), 4.11 (q, 2H), 2.39 (s, 3H), 1.34 (t, 3H).	
446	4-{4-Ethyl-5-[5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine	8.80 (m, 2H), 7.86 (m, 1H), 7.60 (m, 2H), 7.38 (m, 1H), 7.14 (dd, 1H), 4.70 (s, 2H), 4.11 (q, 2H), 2.39 (s, 3H), 1.36 (t, 3H).	398.20

447	3-{4-Ethyl-5-[5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine	8.87 (s, 1H), 8.76 (d, 1H), 8.01 (m, 1H), 7.88 (m, 1H), 7.49 (m, 1H), 7.28 (m, 1H), 7.14 (dd, 1H), 4.69 (s, 2H), 4.07 (q, 2H), 2.39 (q, 2H), 1.35 (t, 3H).	
448	3-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-5-pyridin-4-yl-[1,2,4]triazol-4-ylamine	(DMSO-D6 as solvent): 8.75 (dd, 2H), 8.05 (m, 4H), 7.79 (m, 1H), 7.66 (dd, 1H), 6.33 (s, 2H), 4.65 (s, 2H).	387.05
449	4-{5-[5-(5-Bromo-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.81 (dd, 2H), 8.24 (m, 1H), 7.71 (m, 1H), 7.61 (m, 2H), 7.18 (dd, 1H), 4.72 (s, 2H), 4.13 (m, 2H), 1.29 (m, 3H).	464.02
450	5-(4-Methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-thiophen-2-yl-[1,2,4]oxadiazole	7.75 (m, 2H), 7.51 (m, 3H), 7.16 (m, 1H), 4.64 (s, 2H), 3.70 (s, 3H).	
451	3-[3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzonitrile	8.42 (s, 1H), 8.35 (d, 1H), 7.89 (d, 1H), 7.71 (t, 1H), 7.54 (d, 1H), 7.48 (d, 1H), 7.20 (t, 1H), 4.68 (s, 2H), 4.16 (m, 2H), 1.40 (t, 3H).	395.10
452	3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-phenyl-[1,2,4]oxadiazole	8.13 (d, 2H), 7.49 (br m, 5H), 7.20 (m, 1H), 4.65 (s, 2H), 4.16 (m, 2H), 1.40 (t, 3H).	370.09

453	4-[3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-2-methoxy-pyridine	8.36 (d, 1H), 7.51 (br m, 3H), 7.42 (s, 1H), 7.19 (m, 1H), 4.68 (s, 2H), 4.16 (m, 2H), 1.42 (t, 3H).	
454	3-(3-Chloro-phenyl)-5-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	8.06 (s, 1H), 7.95 (d, 1H), 7.54 (m, 1H), 7.49 (m, 1H), 7.42 (m, 2H), 7.20 (m, 1H), 4.78 (s, 2H), 4.17 (q, 2H), 1.41 (t, 3H).	
455	4-{5-[5-(3-Chloro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.82 (m, 2H), 7.76 (m, 1H), 7.66 (m, 1H), 7.60 (m, 2H), 7.41 (m, 2H), 6.78 (s, 1H), 4.65 (s, 2H), 4.07 (q, 2H), 1.40 (t, 3H).	399.10
456	2-Methyl-4-[3-(4-methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine	8.73 (d, 1H), 7.81 (s, 1H), 7.75 (s, 2H), 7.51 (m, 2H), 4.60 (s, 2H), 3.71 (s, 3H) 2.68 (s, 3H).	
457	4-[3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-2-methyl-pyridine	8.73 (d, 1H), 7.82 (s, 1H), 7.76 (d, 1H), 7.54 (d, 1H), 7.48 (d, 1H), 7.29 (m, 1H), 4.68 (s, 2H), 4.16 (m, 2H), 2.68 (s, 3H), 1.41 (t, 3H).	

458	5-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-thiophen-2-yl-[1,2,4]oxadiazole	7.78 (d, 1H), 7.53 (t, 2H), 7.48 (d, 1H), 7.18 (m, 2H), 4.74 (s, 2H), 4.17 (m, 2H), 1.41 (t, 3H).	376.00
459	4-{5-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.82 (d, 2H), 8.09 (m, 1H), 7.58 (m, 3H), 7.24 (m, 1H), 4.73 (s, 2H), 4.13 (m, 2H), 1.41 (t, 3H).	418.10
460	4-[3-(4-Ethyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-2-methyl-pyridine	8.82 (d, 2H), 8.75 (d, 1H), 7.84 (s, 1H), 7.76 (d, 1H), 7.60 (d, 2H), 4.74 (s, 2H), 4.13 (m, 2H), 1.41 (t, 3H).	
461	3-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-benzonitrile	8.11 (s, 1H), 7.97 (m, 3H), 7.83 (d, 1H), 7.63(m, 3H), 7.50 (t, 1H), 4.63 (s, 2H) and 3.68 (s, 3H)	
462	5-(3-Chloro-phenyl)-3-[5-(3-chloro-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole	8.11 (s, 1H), 8.00 (d, 1H), 7.67(m, 1H), 7.50 (m, 5H), 4.61 (s, 2H) and 3.66 (s, 3H).	
463	5-(3-Chloro-phenyl)-3-[5-(4-chloro-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole	8.11 (s, 1H), 8.01 (d, 1H), 7.55 (m, 6H), 4.61 (s, 2H) and 3.64 (s, 3H).	

464	4-{5-[5-(2,5-Dichloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.80 (dd, 2H), 8.05 (m, 1H), 7.59 (m, 2H), 7.47 (s, 2H), 4.73 (s, 2H), 4.11 (m, 2H), 1.32 (m, 3H).	
465	5-(2,5-Dichloro-phenyl)-3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	8.06 (dd, 1H), 7.50 (m, 4H), 7.19 (dd, 1H), 4.68 (s, 2H), 4.17 (q, 2H), 1.39 (t, 3H).	
466	5-(2,5-Difluoro-phenyl)-3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	8.80 (dd, 2H), 7.79 (m, 1H), 7.60 (m, 2H), 7.28 (m, 1H), 4.68 (s, 2H), 4.11 (q, 2H), 1.39 (t, 3H).	406.10
467	4-{5-[5-(2,5-Difluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine	7.80 (m, 1H), 7.52 (m, 1H), 7.48 (m, 1H), 7.20 (m, 4H), 4.68 (s, 2H), 4.17 (m, 2H), 1.40 (t, 3H).	
468	5-(2,5-Dichloro-phenyl)-3-(4-ethyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	8.07 (dd, 1H), 7.71 (dd, 1H), 7.49 (m, 4H), 4.69 (s, 2H), 4.12 (m, 2H), 1.38 (t, 3H).	
469	5-(2,5-Difluoro-phenyl)-3-(4-ethyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	7.80 (m, 1H), 7.72 (m, 1H), 7.49 (m, 2H), 7.28 (m, 2H), 4.68 (s, 2H), 4.12 (q, 2H), 1.37 (t, 3H).	406.10

470	4-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-propyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.80 (dd, 2H), 8.11 (m, 1H), 7.99 (m, 1H), 7.57 (m, 3H), 7.48 (t, 1H), 4.70 (s, 2H), 3.99 (q, 2H), 1.72 (m, 2H), 0.91 (t, 3H).	
471	4-{5-[5-(2-Fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-propyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.80 (dd, 2H), 7.87 (dd, 1H), 7.58 (m, 2H), 7.39 (m, 1H), 7.15 (q, 1H), 4.70 (s, 2H), 4.01 (m, 2H), 2.40 (s, 3H), 1.70 (m, 2H), 0.87 (t, 3H).	
472	3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-2-yl-[1,2,4]oxadiazole	7.91 (d, 1H), 7.67 (d, 1H), 7.52 (d, 1H), 7.48 (d, 1H), 7.20 (m, 2H), 4.62 (s, 2H), 4.18 (m, 2H), 1.38 (t, 3H).	376.10
473	3-(4-Methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-2-yl-[1,2,4]oxadiazole	7.90 (s, 1H), 7.74 (d, 1H), 7.67 (d, 1H), 7.52 (m, 2H), 7.21 (m, 1H), 4.60 (s, 2H), 3.71 (s, 3H) 2.68 (s, 3H).	
474	4-[4-Methyl-5-(3-thiophen-3-yl-[1,2,4]oxadiazol-5-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine	8.82 (d, 2H), 8.05 (s, 1H), 7.61 (m, 3H), 7.44 (m, 1H), 4.73 (s, 2H), 3.70 (s, 3H).	

475	5-(4-Methyl-5-thiophen-3-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-thiophen-3-yl-[1,2,4]oxadiazole	8.05 (s, 1H), 7.73 (d, 1H), 7.62 (d, 1H), 7.51 (s, 2H), 7.44 (m, 1H), 4.66 (s, 2H), 3.68 (s, 3H).	
476	5-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-thiophen-3-yl-[1,2,4]oxadiazole	8.05 (d, 1H), 7.62 (d, 1H), 7.53 (d, 1H), 7.47 (d, 1H), 7.44 (m, 1H), 7.19 (m, 1H), 4.75 (s, 2H), 4.15 (m, 2H), 1.40 (t, 3H).	376.10
477	5-[3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-thiophene-3-carbonitrile	8.18 (d, 1H), 8.03 (d, 1H), 7.51 (m, 1H), 7.46 (m, 1H), 7.18 (m, 1H), 4.63 (s, 2H), 4.16 (q, 2H), 1.40 (t, 3H).	401.00
478	5-(3-Chloro-phenyl)-3-[5-(2-fluoro-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole	8.13 (s, 1H), 8.01 (d, 1H), 7.52(m, 4H), 7.34 (t, 1H), 7.27 (m, 1H), 4.63 (s, 2H) and 3.54 (s, 3H).	
479	5-(3-Chloro-phenyl)-3-[5-(3-fluoro-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole	8.11 (s, 1H), 8.00 (d, 1H), 7.52(m, 5H), 7.27 (m, 1H), 4.62 (s, 2H) and 3.66 (s, 3H).	403.00
480	5-(3-Chloro-phenyl)-3-[5-(4-fluoro-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole	8.11 (s, 1H), 8.00 (d, 1H), 7.59(m, 4H), 7.49 (t, 1H), 7.22 (m, H), 4.61 (s, 2H) and 3.64 (s, 3H).	403.10

481	3-(5-Benzo[b]thiophen-2-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-chloro-phenyl)-[1,2,4]oxadiazole	8.11 (s, 1H), 8.01 (d, 1H), 7.87(m, 2H), 7.72 (s, 1H), 7.58 (d, 1H), 7.45 (m, 3H), 4.60 (s, 2H) and 3.85 (s, 3H).	
482	5-(3-Chloro-phenyl)-3-[5-(3-methoxy-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole	8.12 (s, 1H), 8.01 (d, 1H), 7.59(dd, 1H), 7.49 (t, 1H), 7.44 (t, 1H), 7.2 (m, 2H), 7.05 (dd, 1H), 4.60 (s, 2H), 3.88 (s, 3H) and 3.65 (s, 3H).	
483	5-(3-Chloro-phenyl)-3-[5-(4-methoxy-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole	8.12 (s, 1H), 8.01 (d, 1H), 7.59(m, 3H), 7.49 (t, 1H), 7.03 (d, 2H), 4.59 (s, 2H), 3.89 (s, 3H) and 3.63 (s, 3H).	415.00
484	3-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazole	7.86 (dd, 1H), 7.59 (m, 1H), 7.37 (m, 1H), 7.14 (m, 2H), 6.58 (q, 1H), 4.63 (s, 2H), 4.26 (q, 2H), 2.39 (s, 3H), 1.37 (t, 3H).	386.10
485	3-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,2,4]oxadiazole	7.91 (m, 2H), 7.59 (m, 1H), 7.40 (m, 2H), 7.10 (q, 1H), 6.58 (q, 1H), 4.61 (s, 2H), 4.24 (q, 2H), 2.43 (s, 3H), 1.36 (t, 3H).	368.20

486	3-(4-Ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazole	7.97 (m, 1H), 7.47 (m, 1H), 7.16 (t, 1H), 4.72 (d, 2H), 4.16 (m, 2H), 2.41 (d, 3H), 1.37 (m,3H).	
487	3-[5-(2-Fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-5-pyridin-4-yl-[1,2,4]triazol-4-ylamine	(CD3OD as solvent):8.72 (m, 2H), 8.17 (m, 2H), 7.86 (dd, 1H), 7.49 (m, 1H), 7.23 (dd, 1H), 4.59 (s, 2H), 2.35 (s, 3H).	
488	3-[5-(2-Fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-5-thiophen-2-yl-[1,2,4]triazol-4-ylamine	(CD3OD as solvent):8.05 (s, 1H), 7.84 (dd, 1H), 7.69 (m, 1H), 7.47 (m, 1H), 7.22 (m, 2H), 4.52 (s, 2H), 2.33 (s, 3H).	
489	3-Pyridin-4-yl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-[1,2,4]triazol-4-ylamine	(CD3OD as solvent):8.73 (dd, 2H), 8.17 (dd, 2H), 7.89 (m, 2H), 7.46 (m, 2H), 4.58 (s, 2H), 2.389 (s, 3H).	
490	3-Thiophen-2-yl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-[1,2,4]triazol-4-ylamine	(CD3OD as solvent):8.05 (dd, 1H), 7.87 (d, 2H), 7.70 (dd, 1H), 7.45 (m, 2H), 7.23 (q, 1H), 4.50 (s, 2H), 2.39 (s, 3H).	

491	3-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-3-yl-[1,2,4]oxadiazole	8.23 (m, 1H), 7.66 (m, 1H), 7.60 (m, 1H), 7.47 (m, 1H), 7.11 (m, 1H), 6.60 (m, 1H), 4.61 (s, 2H), 4.26 (q, 2H), 1.38 (t, 3H).	360.10
492	5-(3-Chloro-phenyl)-3-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	8.11 (m, 1H), 8.00 (m, 1H), 7.59 (m, 2H), 7.51 (t, 1H), 7.12 (m, 1H), 6.60 (m, 1H), 4.63 (s, 2H), 4.26 (q, 2H), 1.38 (t, 3H).	389.00
493	4-[3-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-2-methyl-pyridine	8.73 (d, 1H), 7.82 (s, 1H), 7.75 (m, 1H), 7.60 (m, 1H), 7.12 (m, 1H), 6.60 (m, 1H), 4.65 (s, 2H), 4.26 (q, 2H), 2.68 (s, 3H), 1.39 (t, 3H).	
494	5-(2,5-Difluoro-phenyl)-3-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	7.80 (m, 1H), 7.61 (m, 1H), 7.29 (m, 2H), 7.12 (m, 1H), 6.60 (m, 1H), 4.65 (s, 2H), 4.28 (q, 2H), 1.39 (t, 3H).	390.09
495	4-[4-Ethyl-5-(5-thiophen-3-yl-isoxazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine	8.81 (m, 2H), 7.63 (m, 1H), 7.59 (m, 2H), 7.41 (m, 2H), 6.58 (s, 1H), 4.63 (s, 2H), 4.06 (q, 2H), 1.38 (t, 3H).	371.00

496	4-Ethyl-3-furan-2-yl-5-(5-thiophen-3-yl-isoxazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazole	7.77 (m, 1H), 7.60 (m, 1H) 7.40 (m, 2H), 7.10 (m, 1H), 6.60 (m, 1H), 6.55 (s, 1H), 4.58 (s, 2H), 4.21 (q, 2H), 1.38 (t, 3H).	359.10
497	5-(3-Chloro-phenyl)-3-[5-(3,5-dichloro-phenyl)-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole	8.12 (s, 1H), 8.01 (d, 1H), 7.60(d, 1H), 7.54 (s, 3H), 7.47 (t, 1H), 4.69 (s, 2H),4.06 (q, 2H) and 1.36 (t, 3H).	
498	5-(3-Chloro-phenyl)-3-(4-ethyl-5-p-tolyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	8.13 (s, 1H), 8.01 (d, 1H), 7.53(m, 4H), 7.20 (d, 2H), 4.68 (s, 2H), 4.03 (q, 3H) , 2.45(s, 1H) and 1.32 (t, 3H).	
499	5-(3-Chloro-phenyl)-3-(4-ethyl-5-m-tolyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	8.11 (s, 1H), 8.00 (d, 1H), 7.58(d, 1H), 7.29-7.50(m, 5H), 4.66 (s, 2H), 4.02 (q, 2H), 2.45 (s, 1H) and 1.32 (t, 3H).	
500	5-(3-Chloro-phenyl)-3-[4-ethyl-5-(3-nitro-phenyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole	8.52 (s, 1H), 8.40 (d, 1H), 8.12 (s, 1H), 8.05 (dd, 2H), 7.76(t, 1H),7.60 (d, 1H), 7.50 (t, 1H), 4.72 (s, 2H), 4.10 (q, 2H) and 1.41 (t, 3H).	

501	4-{5-[3-(3-Chloro-phenyl)-isoxazol-5-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine	7.80 (m, 2H), 7.78 (m, 1H), 7.65 (m, 1H), 7.59 (m, 2H), 7.40 (m, 2H), 6.65 (s, 1H), 4.67 (s, 2H), 3.64 (s, 3H).	
502	5-(3-Chloro-phenyl)-3-[5-(2,5-difluoro-phenyl)-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole	8.14 (s, 1H), 8.02 (d, 1H), 7.60(d, 1H), 7.52 (t, 1H), 7.32 (m, 1H), 7.23 (m, 2H), 4.70 (s, 2H), 3.96 (q, 2H) and 1.27 (t, 3H).	
503	5-(3-Chloro-phenyl)-3-[5-(3-chloro-phenyl)-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole	8.11 (s, 1H), 8.06 (d, 1H), 7.63(s, 1H), 7.58 (d, 1H), 7.49 (m, 4H), 7.23 (m, 2H), 4.68 (s, 2H), 4.04 (q, 2H) and 1.34 (t, 3H).	
504	5-(3-Chloro-phenyl)-3-[5-(4-chloro-phenyl)-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole	8.13 (s, 1H), 8.01 (d, 1H), 7.3(m, 6H), 4.68 (s, 2H), 4.03 (q, 2H) and 1.34 (t, 3H).	
505	4-{5-[5-(3-Chloro-phenyl)-oxazol-2-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.78 (d, 2H), 7.55 (m, 3H), 7.44(m, 1H), 7.29 (m, 3H), 4.69 (s, 2H), 4.04 (q, 2H) and 1.34 (t, 3H).	

506	3-[5-(3-Chloro-phenyl)-oxazol-2-ylmethylsulfanyl]-4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazole	7.55 (s, 1H), 7.50 (d, 1H), 7.44(m, 2H), 7.28 (m, 3H), 7.18 (dd, 1H), 4.64 (s, 2H), 4.10 (q, 2H) and 1.35 (t, 3H).	404.00
507	3-[5-(3-Chloro-phenyl)-oxazol-2-ylmethylsulfanyl]-4-ethyl-5-furan-2-yl-4H-[1,2,4]triazole	7.58 (s, 1H), 7.53 (s, 1H), 7.40 (m, 1H), 7.27 (m, 3H), 7.10 (d, 1H), 6.68 (d, 1H), 4.62 (s, 2H), 4.19 (q, 2H) and 1.33 (t, 3H).	388.00
508	5-(2-Chloro-5-methyl-phenyl)-3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	7.83 (s, 1H), 7.53 (d, 1H), 7.44 (m, 2H), 7.32 (d, 1H), 7.18 (t, 2H), 4.63 (s, 2H), 4.17 (q, 2H), 2.37 (s, 3H), 1.38 (t, 3H).	
509	4-{5-[3-(3-Chloro-phenyl)-isoxazol-5-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.80 (m, 2H), 7.78 (m, 1H), 7.66 (m, 1H), 7.57 (m, 2H), 7.41 (m, 2H), 6.67 (s, 1H), 4.71 (s, 2H), 4.03 (q, 2H), 1.36 (t, 3H).	
510	3-[3-(3-Chloro-phenyl)-isoxazol-5-ylmethylsulfanyl]-4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazole	7.78 (s, 1H), 7.64 (m, 1H) 7.52 (m, 1H), 7.41 (m, 3H), 7.18 (m, 1H), 6.65 (s, 1H), 4.66 (s, 2H), 4.08 (q, 2H), 1.36 (t, 3H).	404.00

511	3-[3-(3-Chloro-phenyl)-isoxazol-5-ylmethylsulfanyl]-4-ethyl-5-furan-2-yl-4H-[1,2,4]triazole	7.77 (s, 1H), 7.64 (d, 1H), 7.59 (m, 1H), 7.39 (m, 2H), 7.10 (m, 1H), 6.62 (s, 1H), 6.59 (m, 1H), 4.65 (s, 2H), 4.17 (q, 2H), 1.35 (t, 3H).	388.10
512	4-{5-[5-(2-Fluoro-5-methyl-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine		
513	5-(2,5-Dichloro-thiophen-3-yl)-3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	(DMSO-D6 as solvent): 7.82(dd, 1H), 7.65 (d, 1H), 7.58 (m,1H), 7.25 (m, 1H), 4.60 (s, 2H), 4.16 (q, 2H), 1.24 (t, 3H).	
514	4-{5-[5-(2,5-Dichloro-thiophen-3-yl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.78(d, 2H), 7.71 (d, 2H), 7.68 (m,1H), 4.67 (s, 2H), 4.10 (q, 2H), 1.21 (t, 3H).	
515	4-{4-Ethyl-5-[5-(2-fluoro-5-methyl-phenyl)-isoxazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine	8.81 (m, 2H), 7.73 (m, 1H), 7.60 (m, 2H), 7.21 (m, 1H), 7.07 (m, 1H), 6.76 (m, 1H), 4.63 (s, 2H), 4.02 (q, 2H), 2.40 (s, 3H), 1.38 (t, 3H).	

516	4-Ethyl-3-[5-(2-fluoro-5-methyl-phenyl)-isoxazol-3-ylmethylsulfanyl]-5-thiophen-2-yl-4H-[1,2,4]triazole	7.71 (d, 1H), 7.53 (m, 1H), 7.47 (m, 1H), 7.46 (m, 2H), 7.07 (m, 1H), 6.77 (d, 1H), 4.63 (s, 2H), 4.12 (q, 2H), 2.40 (s, 3H), 1.39 (t, 3H).	
517	4-Ethyl-3-[5-(2-fluoro-5-methyl-phenyl)-isoxazol-3-ylmethylsulfanyl]-5-furan-2-yl-4H-[1,2,4]triazole	7.72 (d, 1H), 7.60 (m, 1H), 7.10 (m, 1H), 7.05 (m, 2H), 6.77 (d, 1H), 6.60 (m, 1H), 4.61 (s, 2H), 4.21 (q, 2H), 2.39 (s, 3H), 1.38 (t, 3H).	
518	5-(3-Chloro-phenyl)-3-(4-ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	8.11 (s, 1H), 8.01 (d, 1H), 7.60 (d, 1H), 7.50 (t, 1H), 4.72(s, 2H), 4.12 (q, 2H) and 1.42 (t, 3H).	391.00
519	3-(3-Chloro-phenyl)-5-(4-ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	8.05 (s, 1H), 7.94 (d, 1H), 7.50 (d, 1H), 7.43 (t, 1H), 4.83(s, 2H), 4.13 (q, 2H) and 1.44 (t, 3H).	
520	3-(4-Ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-3-yl-[1,2,4]oxadiazole	8.23 (s, 1H), 7,65 (d, 1H), 7.48 (m, 1H), 4.69 (s, 2H), 4.12 (q, 2H) and 1.41 (t, 3H).	
521	5-(4-Ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-thiophen-3-yl-[1,2,4]oxadiazole	8.05 (s, 1H), 7,61 (d, 1H), 7.43 (m, 1H), 4.81 (s, 2H), 4.12 (q, 2H) and 1.43 (t, 3H).	

522	5-(3-Chloro-phenyl)-3-[4-ethyl-5-(3-fluoro-phenyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole	8.12 (d, 1H), 8.00 (d, 1H), 7.52 (m, 4H), 7.25 (m, 2H), 4.67 (s, 2H), 4.06 (q, 2H), 1.31 (t, 3H).	
523	5-(3-Chloro-phenyl)-3-[4-ethyl-5-(4-fluoro-phenyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole	8.10 (s, 1H), 7.99 (d, 1H), 7.59 (m, 4H), 7.48 (t, 1H), 7.22 (d, 1H), 4.67 (s, 2H), 4.01 (q, 2H), 1.30 (t, 3H).	
524	3-(4-Ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-thiophen-2-yl-[1,2,4]oxadiazole	7.91 (s, 1H), 7,68 (d, 1H), 7.21 (m, 1H), 4.67 (s, 2H), 4.13 (q, 2H) and 1.41 (t, 3H).	
525	3-{3-[5-(3-Chloro-thiophen-2-yl)-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazol-5-yl}-benzonitrile	8.35(m, 2H), 7.89 (d, 1H), 7.87 (t, 1H), 7.58 (d,1H), 7.09 (d,1H), 4.70 (s, 2H), 4.00 (q, 2H), 1.27 (t, 3H).	
526	4-{5-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.82 (d, 2H), 8.01 (d, 1H), 9.93 (m, 1H), 7.59 (m, 2H), 7.52 (m, 1H), 7.47 (m, 1H), 4.83 (s, 2H), 4.11 (q, 2H), 1.40 (t, 3H).	400.10

527	2-(3-Chloro-phenyl)-5-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazole	8.00 (s, 1H), 7.89 (d, 1H), 7.60 (m, 1H), 7.50 (m, 1H), 7.44 (m, 1H), 7.13 (m, 1H), 6.60 (m, 1H), 4.76 (s, 2H), 4.25 (q, 2H), 1.38 (t, 3H).	389.00
528	5-(3-Chloro-phenyl)-3-[4-ethyl-5-(4-methoxy-phenyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole	8.12 (s, 1H), 8.01 (d, 1H), 7.57 (m, 3H), 7.51 (t, 1H), 7.05 (d, 2H), 4.67 (s, 2H), 4.02 (q, 2H), 3.89 (s, 3H), 1.31 (t, 3H).	
529	5-(3-Chloro-phenyl)-3-[5-(2-fluoro-5-methyl-phenyl)-4-furan-2-ylmethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole	8.12 (s, 1H), 8.02 (d, 1H), 7.58 (d, 1H), 7.52 (d, 1H), 7.35 (d, 2H), 7.23 (s, 1H), 7.22 (d, 1H), 6.19 (s, 1H), 6.04 (s, 1H), 5.13 (s, 2H), 4.61 (s, 2H), 2.37 (s, 3H).	
530	4-[3-(4-Ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-2-methyl-pyridine	8.74 (d, 1H), 7,81 (s, 1H), 7.74 (d, 1H), 4.74 (s, 2H), 4.12 (q, 2H) 2.69 (s,1H) and 1.42 (t, 3H).	
531	3-(4-Ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-methoxy-phenyl)-[1,2,4]oxadiazole	7.70 (d, 1H), 7,60 (s, 1H), 7.44 (t, 1H), 7.16 (d, 1H), 4.70 (s, 2H), 4.12 (q, 2H), 3.90 (s, 3H) and 1.41 (t, 3H).	

532	5-(4-Ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-(3-methoxy-phenyl)-[1,2,4]oxadiazole	7.63 (d, 1H), 7,56 (s, 1H), 7.39 (t, 1H), 7.07 (d, 1H), 4.82 (s, 2H), 4.12 (q, 2H) and 1.42 (t, 3H).	
533	5-(4-Ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-thiophen-2-yl-[1,2,4]oxadiazole	7.77 (s, 1H), 7,52 (d, 1H), 7.16 (m, 1H), 4.79 (s, 2H), 4.13 (q, 2H) and 1.42 (t, 3H).	
534	5-(5-Chloro-2-fluoro-phenyl)-3-(4-ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	8.07 (dd, 1H), 7.56 (m, 1H), 7.24 (dd, 1H), 4.73 (s, 2H), 4.13 (q, 2H) and 1.42 (t, 3H).	
535	3-[3-(4-Ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzonitrile	8.40 (s, 1H), 8.34 (d, 1H), 7.91 (d, 1H), 7.01 (t, 1H), 4.73 (s, 2H), 4.12 (q, 2H) and 1.42 (t, 3H).	381.10
536	3-[5-(3-Chloro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-ethyl-5-trifluoromethyl-4H-[1,2,4]triazole	7.75 (s, 1H), 7.63 (m, 1H), 7.40 (m, 2H), 6.73 (s, 1H), 4.65 (s, 2H), 4.07 (q, 2H) and 1.40 (t, 3H).	
537	3-[5-(3-Chloro-phenyl)-oxazol-2-ylmethylsulfanyl]-4-ethyl-5-trifluoromethyl-4H-[1,2,4]triazole	7.58 (s, 1H), 7.46 (d, 1H), 7.32 (d, 3H), 4.74 (s, 2H), 4.09 (q, 2H) and 1.39 (t, 3H).	

538	4-Ethyl-3-(5-thiophen-3-yl-isoxazol-3-ylmethylsulfanyl)-5-trifluoromethyl-4H-[1,2,4]triazole	7.78 (s, 1H), 7.39 (m, 1H), 6.53 (d, 1H), 4.63 (s, 2H), 4.07 (q, 2H) and 1.39 (t, 3H).	
539	4-{3-[5-(3-Fluoro-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazol-5-yl}-2-methyl-pyridine	8.73 (d, 1H), 7.83 (s, 1H), 7.76 (d, 1H), 7.47 (m, 3H), 7.27 (s, 1H), 4.65 (s, 2H), 3.67 (s, 3H), 2.69 (s, 3H).	
540	4-{3-[5-(3-Chloro-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazol-5-yl}-2-methyl-pyridine	8.74 (d, 1H), 7.82 (s, 1H), 7.67 (d, 1H), 7.56 (d, 1H), 7.51 (m, 1H), 7.48 (m, 1H), 7.46 (s, 1H), 4.65 (s, 2H), 3.67 (s, 3H), 2.69 (s, 3H).	
541	4-{3-[5-(4-Chloro-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazol-5-yl}-2-methyl-pyridine	8.73 (d, 1H), 7.82 (s, 1H), 7.75 (d, 1H), 7.63 (d, 2H), 7.51 (d, 2H), 4.65 (s, 2H), 3.65 (s, 3H), 2.69 (s, 3H).	
542	4-{3-[5-(4-Methoxy-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazol-5-yl}-2-methyl-pyridine	8.73 (d, 1H), 7.83 (s, 1H), 7.45 (d, 1H), 7.61 (d, 2H), 7.04 (d, 2H), 4.62 (s, 2H), 3.89 (s, 3H), 3.64 (s, 3H), 2.69 (s, 3H).	

543	4-[3-(4-Ethyl-5-p-tolyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-2-methyl-pyridine	8.74 (d, 1H), 7.85 (s, 1H), 7.77 (d, 1H), 7.51 (d, 2H), 7.32 (d, 2H), 4.70 (s, 2H), 4.03 (q, 2H), 2.70 (s, 3H), 2.45 (s, 3H), 1.31 (t, 3H).	
544	3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-fluoro-phenyl)-[1,2,4]oxadiazole	(DMSO-D6 as solvent): 7.93(m, 1H), 7.86 (m, 2H), 7.80 (m,1H), 7.67 (m, 2H), 7.25 (m,1H), 4.61 (s, 2H), 4.16 (q, 2H), 1.24 (t, 3H).	388.10
545	4-{4-Ethyl-5-[5-(3-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine	8.78(bs, 2H), 7.92 (m, 2H), 7.71 (d, 2H), 7.68 (m,1H), 7.27 (m,1H), 4.70 (s, 2H), 4.10 (q, 2H), 1.39 (t, 3H).	383.10
546	5-(3-Chloro-phenyl)-3-[5-(3,5-difluoro-phenyl)-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole	8.11 (s, 1H), 8.01 (d, 1H), 7.58 (d, 1H), 7.50 (t, 1H), 7.21 (m, 2H), 7.00 (t, 1H), 4.68 (s, 2H), 4.07 (q, 2H), 1.35 (t, 3H).	
547	5-(3-Chloro-phenyl)-3-[5-(2,6-difluoro-phenyl)-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole	8.12 (s, 1H), 8.02 (d, 1H), 7.59 (m, 2H), 7.52 (d, 1H), 7.41 (d, 1H), 7.04 (d, 1H), 4.73 (s, 2H), 4.21 (q, 2H), 1.42 (t, 3H).	

548	2-[3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-4-methyl-phenol	9.89 (s, 1H), 7.70 (s, 1H), 7.56 (d, 1H), 7.54 (d, 1H), 7.30 (m, 1H), 7.18 (m, 1H), 6.98 (d, 1H), 4.66 (s, 2H), 4.12 (q, 2H), 2.34 (s, 3H), 1.37 (t, 3H).	399.90
549	3-{1-[5-(3-Chloro-phenyl)-isoxazol-3-yl]-ethylsulfanyl}-4-ethyl-5-furan-2-yl-4H-[1,2,4]triazole	7.73 (bs, 1H), 7.59 (m, 2H), 7.41 (m, 2H), 7.10 (dd, 1H), 6.59 (m, 2H), 5.05 (q, 1H), 4.13 (q, 2H), 1.91 (d, 3H), 1.27 (t, 3H).	401.10
550	4-(5-{1-[5-(3-Chloro-phenyl)-isoxazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyridine	8.8 (dd, 2H), 7.74 (bs, 1H), 7.63 (m, 1H), 7.57 (dd, 2H), 7.40 (m, 2H), 6.62 (s, 2H), 5.15 (q, 1H), 4.05 (q, 2H), 1.95 (d, 3H), 1.34 (t, 3H).	
551	3-[5-(4-Butoxy-phenyl)-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-5-(3-chloro-phenyl)-[1,2,4]oxadiazole	8.12 (s, 1H), 8.01 (d, 1H), 7.58 (d, 1H), 7.52 (d, 2H), 7.49 (d, 1H), 7.01 (d, 2H), 4.69 (s, 2H), 4.02 (q, 4H), 1.82 (m, 2H), 1.51 (q, 2H), 1.32 (t, 3H), 1.01 (t, 3H).	

552	3-(5-Benzo[1,3]dioxol-5-yl-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-chloro-phenyl)-[1,2,4]oxadiazole	8.12 (s, 1H), 8.00 (d, 1H), 7.58 (d, 1H), 7.51 (d, 1H), 7.09 (d, 2H), 6.96 (s, 1H), 6.08 (s, 2H), 4.67 (s, 2H), 4.02 (q, 2H), 1.31 (t, 3H).	
553	3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(2-methyl-thiazol-4-yl)-[1,2,4]oxadiazole	8.11 (s, 1H), 7.48 (m, 2H), 7.16 (t, 1H), 4.63 (s, 2H), 4.13 (q, 2H), 2.82 (s, 3H), 1.37 (t, 3H).	391.90
554	3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(4-fluoro-phenyl)-[1,2,4]oxadiazole	(DMSO-D6 as solvent): 8.21(m, 2H), 7.51 (m, 2H), 7.21 (m,3H), 4.63 (s, 2H), 4.16 (q, 2H), 1.38 (t, 3H).	
555	4-Ethyl-3-{1-[5-(2-fluoro-5-methyl-phenyl)-isoxazol-3-yl]-ethylsulfanyl}-5-furan-2-yl-4H-[1,2,4]triazole	7.71 (dd, 1H), 7.59 (dd, 1H), 7.26 (m, 1H), 7.06 (m, 2H), 6.66 (d, 1H), 6.58 (dd, 1H), 5.06 (q, 1H), 4.13 (q, 2H), 2.39 (s, 3H), 1.91 (d, 3H), 1.28 (t, 3H).	
556	4-(4-Ethyl-5-{1-[5-(2-fluoro-5-methyl-phenyl)-isoxazol-3-yl]-ethylsulfanyl}-4H-[1,2,4]triazol-3-yl)-pyridine	8.79 (dd, 2H), 7.71 (dd, 1H), 7.59 (dd, 2H), 7.23 (m, 1H), 7.06 (m, 1H), 6.64 (d, 1H), 5.15 (q, 1H), 4.01 (q, 2H), 2.39 (s, 3H), 1.94 (d, 3H), 1.30 (t, 3H).	410.10

557	5-(3-Chloro-phenyl)-3-[4-ethyl-5-(3-methyl-3H-imidazol-4-yl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole	8.11 (s, 1H), 8.00 (d, 1H), 7.66 (s, 1H), 7.58 (d, 1H), 7.52 (t, 1H), 7.37 (s, 1H), 4.69 (s, 2H), 4.09 (q, 2H), 3.93 (s, 3H), 1.37 (t, 3H).	
558	5-(3-Chloro-phenyl)-3-[4-ethyl-5-(1-methyl-1H-imidazol-2-yl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole	8.12 (s, 1H), 8.01 (d, 1H), 7.57 (d, 1H), 7.51 (t, 1H), 7.17 (s, 1H), 7.04 (s, 1H), 4.69 (s, 2H), 4.56 (q, 2H), 4.12 (s, 3H), 1.40 (t, 3H).	
559	5-(3-Chloro-phenyl)-3-[4-ethyl-5-(1-methyl-1H-imidazol-4-yl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole	8.12 (s, 1H), 8.01 (d, 1H), 7.65 (s, 1H), 7.57 (d, 1H), 7.48 (d, 2H), 4.60 (s, 2H), 4.50 (q, 2H), 3.79 (s, 3H), 1.36 (t, 3H).	
560	4-{5-[5-(3-Chloro-phenyl)-4-methyl-isoxazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.81 (bs, 2H), 7.70 (m, 1H), 7.61 (m, 3H), 7.44 (m, 2H), 4.65 (s, 2H), 4.09 (q, 2H), 2.31 (s, 3H), 1.40 (t, 3H).	
561	3-[5-(3-Chloro-phenyl)-4-methyl-isoxazol-3-ylmethylsulfanyl]-4-ethyl-5-furan-2-yl-4H-[1,2,4]triazole	7.70 (s, 1H), 7.60 (m, 2H), 7.43 (m, 2H), 7.10 (m, 1H), 6.59 (m, 1H), 4.59 (s, 2H), 4.23 (q, 2H), 2.28 (s, 3H), 1.38 (t, 3H).	

562	3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(4-methyl-thiophen-2-yl)-[1,2,4]oxadiazole	7.61(d, 1H), 7.49 (m, 2H), 7.22 (m,2H), 4.59 (s, 2H), 4.16 (q, 2H),2.32 (s,3H), 1.38 (t, 3H).	
563	5-(3-Chloro-phenyl)-3-[4-ethyl-5-(3-methyl-thiophen-2-yl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole	8.13 (s, 1H), 8.01 (d, 1H), 7.58 (d, 1H), 7.52 (d, 1H), 7.45 (d, 1H), 7.02 (d, 1H), 4.69 (s, 2H), 3.97 (q, 2H), 2.32 (s, 3H), 1.28 (t, 3H).	
564	5-(3-Chloro-phenyl)-3-[4-ethyl-5-(5-methyl-thiophen-2-yl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole	8.11 (s, 1H), 8.01 (d, 1H), 7.58 (d, 1H), 7.51 (t, 1H), 7.28 (s, 1H), 6.83 (d, 1H), 4.64 (s, 2H), 4.14 (q, 2H), 2.56 (s, 3H), 1.39 (t, 3H).	
565	4-{5-[4-Chloro-5-(3-chloro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.81 (d, 2H), 7.99 (m, 1H), 7.90 (m, 1H), 7.60 (m, 2H), 7.48 (m, 2H), 4.65 (s, 2H), 4.10 (q, 2H), 1.39 (t, 3H).	
566	3-[4-Chloro-5-(3-chloro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-ethyl-5-furan-2-yl-4H-[1,2,4]triazole	7.99 (s, 1H), 7.90 (m, 1H), 7.60 (m, 1H), 7.47 (m, 2H), 7.12 (m, 1H), 6.60 (m, 1H), 4.59 (s, 2H), 4.25 (q, 2H), 1.38 (t, 3H).	

567	2-Chloro-4-{5-[5-(3-chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-6-methyl-pyridine	8.11 (s, 1H), 8.00 (d, 1H), 7.58 (d, 1H), 7.52 (d, 1H), 7.40 (d, 2H), 4.71 (s, 2H), 4.10 (q, 2H), 2.64 (s, 3H), 1.40 (t, 3H).	
568	3-[5-(5-Bromo-furan-2-yl)-4-ethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-5-(3-chloro-phenyl)-[1,2,4]oxadiazole	8.11 (s, 1H), 7.99 (d, 1H), 7.58 (d, 1H), 7.51 (t, 1H), 7.07 (d, 1H), 6.52 (d, 1H), 4.64 (s, 2H), 4.23 (q, 2H), 1.40 (t, 3H).	
569	2-Chloro-4-{5-[5-(3-chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.59 (d, 1H), 8.10 (s, 1H), 8.00 (d, 1H), 7.66 (s, 1H), 7.59 (d, 1H), 7.54 (d, 1H), 7.50 (d, 1H), 4.72 (s, 2H), 4.11 (q, 2H), 1.42 (t, 3H).	
570	2-Chloro-4-{5-[5-(3-chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-6-methoxy-pyridine	8.11 (s, 1H), 8.00 (d, 1H), 7.58 (d, 1H), 7.50 (t, 1H), 7.24 (s, 1H), 6.91 (s, 1H), 4.70 (s, 2H), 4.08 (q, 2H), 4.02 (s, 3H), 1.39 (t, 3H).	464.10
571	2-[3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-4-methyl-benzonitrile	8.02 (s, 1H), 7.76 (d, 2H), 7.47 (m,3H), 7.17 (t, 1H), 4.68 (s, 2H), 4.19 (q, 2H), 2.51 (s, 3H), 1.39 (t, 3H).	

572	5-(3-Chloro-phenyl)-3-[4-ethyl-5-(3-methoxy-thiophen-2-yl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole	8.14 (s, 1H), 8.03 (d, 1H), 7.58 (d, 1H), 7.50 (d, 1H), 7.44 (d, 1H), 6.94 (1H), 4.67 (s, 2H), 4.03 (q, 2H), 3.88 (s, 3H), 1.29 (t, 3H).	
573	3-[5-(5-Chloro-thiophen-3-yl)-isoxazol-3-ylmethylsulfanyl]-4-ethyl-5-furan-2-yl-4H-[1,2,4]triazole	7.61 (m, 1H), 7.52 (d, 1H), 7.21 (d, 1H), 7.11 (m, 1H), 7.61 (m, 1H), 6.55 (s, 1H), 4.57 (s, 2H), 4.21 (q, 2H), 1.38 (t, 3H).	393.10
574	3-[3-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-5-fluoro-benzonitrile	8.21(m, 1H), 8.04 (dd, 1H), 7.59 (m, 2H), 7.10 (dd,1H), 6.59 (dd,1H), 4.64 (s, 2H), 4.25 (q, 2H), 1.38 (t, 3H).	
575	4-Ethyl-3-(5-phenyl-isoxazol-3-ylmethylsulfanyl)-5-thiophen-2-yl-4H-[1,2,4]triazole	7.77 (m, 2H), 7.53 (d, 1H), 7.47 (m, 4H), 7.19 (dd, 1H), 6.71 (s, 1H), 4.61 (s, 2H), 4.12 (q, 2H) and 1.39 (t, 3H).	
576	4-Methyl-3-(5-phenyl-isoxazol-3-ylmethylsulfanyl)-5-thiophen-3-yl-4H-[1,2,4]triazole	7.77 (m, 3H), 7.50 (m, 5H), 6.69 (s, 1H), 4.56 (s, 2H) and 3.67 (s, 3H)	

577	4-Ethyl-3-furan-2-yl-5-(5-phenyl-isoxazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazole	7.77 (m, 2H), 7.61 (s, 1H), 7.46 (m, 3H), 7.14 (d, 1H), 6.69 (s, 1H), 6.60 (d, 1H), 4.60 (s, 2H), 4.22 (q, 2H) and 1.38 (t, 3H).	
578	4-[4-Ethyl-5-(5-phenyl-isoxazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine	8.82 (w, 2H), 7.77 (m, 2H), 7.61 (d, 2H), 7.45 (m, 3H), 6.71 (s, 1H), 4.65 (s, 2H), 4.06 (q, 2H) and 1.39 (t, 3H).	
579	4-[4-Methyl-5-(5-phenyl-isoxazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine	8.81 (w, 2H), 7.77 (m, 2H), 7.63 (d, 2H), 7.46 (m, 3H), 6.70 (s, 1H), 4.60 (s, 2H) and 3.68 (s, 3H).	
580	2-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-m-tolyl-[1,3,4]oxadiazole	7.80 (m, 2H), 7.70 (m, 1H), 7.35(m, 2H), 7.13 (m, 2H), 6.60 (m, 1H), 4.74 (s, 2H), 4.23 (q, 2H), 2.40 (s, 3H), 1.36 (t, 3H).	368.10
581	4-[4-Methyl-5-(5-m-tolyl-[1,3,4]oxadiazol-2-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine	8.81 (m, 2H), 7.80 (m, 2H), 7.61 (d, 2H), 7.39 (m, 2H), 4.74 (s, 2H), 3.71 (s, 3H), 2.4 (s, 3H).	365.10

582	4-[4-Ethyl-5-(5-m-tolyl-[1,3,4]oxadiazol-2-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine	8.81 (d, 2H), 7.81 (m, 2H), 7.58 (m, 2H), 7.37 (m, 2H), 4.81 (s, 2H), 4.41 (q, 2H), 2.42 (s, 3H), 1.33 (t, 3H).	379.10
583	4-{5-[5-(5-Chloro-thiophen-3-yl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.80 (d, 2H), 7.98 (m, 1H), 7.58 (d, 2H), 7.46 (d,1H), 4.66 (s, 2H), 4.10 (q, 2H), 1.38 (t,3H).	405.90
584	3-[3-(4-Ethyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-4-fluoro-benzonitrile	8.79 (bs, 2H), 8.46 (m, 1H), 7.91 (m, 1H), 7.59 (d,2H), 7.43 (t, 1H), 4.74 (s, 2H), 4.12 (q, 2H), 1.41 (t,3H).	
585	3-[3-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-4-fluoro-benzonitrile	8.45(dd, 1H), 7.91 (m, 1H), 7.59 (d, 1H), 7.43 (t, 1H), 7.10 (d,1H), 6.58 (dd,1H), 4.65 (s, 2H), 4.27 (q, 2H), 1.39 (t, 3H).	397.10
586	3-[3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-4-fluoro-benzonitrile	8.45 (dd, 1H), 7.90 (m, 1H), 7.47 (m,3H), 7.18 (t, 1H), 4.68 (s, 2H), 4.17 (q, 2H), 1.41 (t, 3H).	

587	3-[3-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzonitrile	8.41 (m, 2H), 7.89 (d, 1H), 7.69 (d, 1H), 7.13 (m, 1H), 6.60 (m, 1H), 4.65 (s, 2H), 4.27 (q, 2H), 1.40 (t, 3H).	379.10
588	3-[5-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-3-yl]-benzonitrile	8.36 (m, 2H), 7.80 (t, 1H), 7.62 (m, 2H), 7.15 (m, 1H), 6.61 (m, 1H), 4.78 (s, 2H), 4.2 (q, 2H), 1.40 (t, 3H).	379.10
589	3-[3-(4-Methyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzonitrile	8.41 (m, 2H), 7.90 (m, 1H), 7.72 (t, 1H), 4.68 (s, 2H), 3.73 (s, 3H).	
590	5-(5-Chloro-2-fluoro-phenyl)-3-(4-methyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	8.08 (m, 1H), 7.58 (m, 1H), 7.25 (m, 1H), 4.67 (s, 2H), 3.74 (s, 3H).	394.90
591	2-Chloro-4-[3-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine	8.63 (m, 1H), 8.02 (m, 1H), 7.89 (m, 1H), 7.61 (m, 1H), 7.14 (m, 1H), 6.61 (m, 1H), 4.67 (s, 2H), 4.27 (q, 2H), 1.40 (t, 3H).	390.00
592	2-Chloro-4-[3-(5-furan-2-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine	8.63 (d, 1H), 8.00 (d, 1H), 7.88 (m, 1H), 7.62 (d, 1H), 7.14 (d, 1H), 6.61 (m, 1H), 4.60 (s, 2H), 3.82 (s, 3H).	

593	2-(3-Chloro-phenyl)-5-[4-methyl-5-(2-methyl-thiazol-4-yl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,3,4]oxadiazole	7.98 (m, 2H), 7.89 (d, 1H), 7.49 (m, 1H), 7.44 (m, 1H), 4.69 (s, 2H), 3.92 (s, 3H), 2.77 (s, 3H).	
594	2-(3-Chloro-phenyl)-5-(4-methyl-5-thiazol-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazole	8.91 (s, 1H), 8.24 (s, 1H), 7.98 (s, 1H), 7.91 (d, 1H), 7.49 (m, 1H), 7.43 (m, 1H), 4.72 (s, 2H), 3.96 (s, 3H).	
595	2-(3-Chloro-phenyl)-5-(5-furan-2-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazole	8.00 (s, 1H), 7.89 (d, 1H), 7.60 (s, 1H), 7.53 (m, 1H), 7.43 (m, 1H), 7.12 (d, 1H), 6.60 (d of d, 1H), 4.68 (s, 2H), 3.80 (s, 3H).	
596	2-(3-Chloro-phenyl)-5-(4-ethyl-5-trifluoromethyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazole	8.00 (s, 1H), 7.90 (d, 1H), 7.52 (m, 2H), 4.86 (s, 2H), 4.13 (q, 2H), 1.42 (t, 3H).	
597	4-{4-Ethyl-5-[5-(4-methyl-thiophen-2-yl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine	8.79 (d, 2H), 7.68 (s, 1H), 7.59 (d, 2H), 7.23 (m,1H), 4.63 (s, 2H), 4.10 (q, 2H), 2.32 (d,3H), 1.37 (t,3H).	

598	3-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(4-methyl-thiophen-2-yl)-[1,2,4]oxadiazole	7.67 (d, 1H), 7.59 (m, 1H), 7.2 (s, 1H), 7.09 (d, 1H), 6.58 (dd,1H), 4.56 (s, 2H), 4.24 (q, 2H), 2.32 (s, 3H), 1.36 (t, 3H).	374.00
599	3-(3-Chloro-phenyl)-5-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	8.02 (m, 1H), 7.91 (m, 1H), 7.57 (d, 1H), 7.35 (m, 2H), 7.08 (d, 1H), 6.56 (dd,1H), 4.72 (s, 2H), 4.22 (q, 2H), 2.32 (s, 3H), 1.36 (t, 3H).	
600	4-{5-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.79 (dd, 2H), 8.02 (m,1H), 7.92 (m, 1H), 7.57 (dd, 2H), 7.42 (m,2H), 4.80 (s, 2H), 4.08 (q, 2H), 1.38 (t,3H).	
601	4-{4-Ethyl-5-[5-(3-nitro-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine	8.87 (m, 3H), 8.42 (m, 2H), 7.75 (t, 1H), 7.66 (d, 2H), 4.88 (s, 2H), 4.15 (q, 2H), 1.45 (t, 3H).	
602	2-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-nitro-phenyl)-[1,3,4]oxadiazole	8.87 (t, 1H), 8.39 (m, 2H), 7.73 (t, 1H), 7.61 (m, 1H), 7.15 (m, 1H), 6.61 (m, 1H), 4.28 (q, 2H), 1.78 (s, 2H), 1.41 (t, 3H).	

603	4-{5-[5-(3-Chloro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-cyclopropyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.79 (d, 2H), 7.78 (m, 3H), 7.66 (m, 1H), 7.39 (m, 2H), 6.84 (s, 1H), 4.69 (s, 2H), 3.27 (m, 1H), 1.20 (q, 2H), 0.83 (m, 2H).	411.00
604	3-[5-(3-Chloro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-ethyl-5-(4-methoxy-phenyl)-4H-[1,2,4]triazole	7.77 (m, 1H), 7.65 (m, 1H), 7.56 (m, 2H), 7.41 (m, 2H), 7.04 (m, 2H), 6.79 (s, 1H), 4.61 (s, 2H), 3.97 (q, 2H), 3.89 (s, 3H), 1.32 (t, 3H).	428.20
605	5-(3-Chloro-phenyl)-3-[1-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,2,4]oxadiazole	8.08 (m, 1H), 7.96 (dd, 1H), 7.45 (m, 4H), 7.17 (m, 1H), 4.93 (q, 1H), 3.67 (s, 3H), 1.91 (d,3H).	404.92
606	5-(3-Chloro-phenyl)-3-[1-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,2,4]oxadiazole	8.1(d, 1H), 7.98 (d, 1H), 7.51 (m,4H), 7.17 (t, 1H), 5.11 (q, 1H), 4.11 (q, 2H), 1.93 (d,3H), 1.34 (t, 3H).	418.90
607	4-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine	8.79 (dd, 2H), 8.08 (m,1H), 7.98 (dd, 1H), 7.59 (m, 3H), 7.46 (t, 1H), 5.05 (q, 1H), 3.66 (s, 3H), 1.94 (d, 3H).	400.07

608	4-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyridine	8.79 (dd, 2H), 8.10 (m,1H), 7.99 (dd, 1H), 7.58 (m, 3H), 7.47 (t, 1H), 5.20 (q, 1H), 4.06 (q, 2H), 1.96 (d, 3H), 1.33 (t,3H).	414.05
609	3-[5-(4-Ethyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-benzonitrile	8.84 (s, 2H), 8.30 (m, 2H), 7.85 (m, 1H), 7.66 (m, 3H), 4.84 (s, 2H), 4.14 (q, 2H), 1.43 (t, 3H).	
610	3-[5-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-benzonitrile	8.27 (m, 2H), 7.82 (m, 1H), 7.62 (m, 2H), 7.18 (t, 1H), 6.62 (m, 1H), 4.79 (s, 2H), 4.27 (q, 2H), 1.40 (t, 3H).	
611	3-[5-(4-Methyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-benzonitrile	8.83 (d, 2H), 8.31 (m, 2H), 7.84 (m, 4H), 4.81 (s, 2H), 3.77 (s, 3H).	
612	3-[5-(4-Cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-benzonitrile	8.82 (s, 2H), 8.33 (m, 2H), 7.86 (t, 3H), 7.67 (t, 1H), 4.91 (d, 2H), 1.24 (m, 3H), 0.88 (m, 2H).	402.20
613	4-{5-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine	(CD3OD as solvent): 8.80 (s (br), 2H), 7.96 (m, 2H), 7.81(d,2H), 7.61 (m, 2H), 4.73 (s, 2H), 3.84 (s, 3H).	

614	4-{5-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4-cyclopropyl-4H-[1,2,4]triazol-3-yl}-pyridine	(CD3OD as solvent): 8.75 (d, 2H), 8.02 (s, 1H), 7.96 (d, 1H), 7.89 (d, 2H), 7.60 (m, 2H), 4.89 (s, 2H), 3.59 (m, 1H), 1.21 (m, 2H), 0.84 (m, 2H).	412.16
615	4-{5-[5-(5-Chloro-2-fluoro-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4-cyclopropyl-4H-[1,2,4]triazol-3-yl}-pyridine	7.80 (m, 2H), 8.04 (m, 1H), 7.77 (d, 2H), 7.51 (m, 1H), 7.21 (t, 1H), 4.92 (s, 2H), 3.32 (m, 1H), 1.21 (m, 2H), 0.85 (m, 2H).	430.11
616	2-(5-Chloro-2-fluoro-phenyl)-5-[4-ethyl-5-(4-methoxy-phenyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,3,4]oxadiazole	8.02 (m, 1H), 7.52 (m, 3H), 7.20 (t, 1H), 7.04 (m, 2H), 4.81 (s, 2H), 4.03 (q, 2H), 3.89 (s, 3H), 1.33 (t, 3H).	
617	4-{5-[5-(5-Chloro-2-fluoro-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.83 (d, 2H), 8.03 (m, 1H), 7.65 (m, 2H), 7.51 (m, 1H), 7.20 (t, 1H), 4.78 (s, 2H), 3.75 (s, 3H).	
618	4-{5-[5-(5-Chloro-2-fluoro-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.82 (bs, 2H), 8.02 (m, 1H), 7.61 (m, 2H), 7.51 (m, 1H), 7.20 (t, 1H), 4.85 (s, 2H), 4.13 (q, 2H), 1.41 (t, 3H).	

619	2-(3-Chloro-phenyl)-5-[4-ethyl-5-(4-methoxy-phenyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,3,4]oxadiazole	8.01 (d of d collapsed, 1H), 7.85 (d, 1H), 7.51(m, 4H), 7.00(d, 2H), 4.79 (s, 2H), 4.00 (q, 2H), 3.88 (s, 3H), 1.30 (t, 3H).	
620	2-(3-Chloro-phenyl)-5-[1-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,3,4]oxadiazole	7.97 (s, 1H), 7.84 (d, 1H), 7.58 (d, 1H), 7.49 (m, 1H), 7.40 (m, 1H), 7.12 (d, 1H), 6.59 (d of d, 1H), 5.16 (q, 1H), 4.17 (q, 2H), 2.02 (d, 3H), 1.28 (t, 3H).	
621	5-(5-Chloro-2-fluoro-phenyl)-3-[1-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,2,4]oxadiazole	8.06 (m, 1H), 7.54 (m, 3H), 7.23 (m, 2H), 4.93 (q, 1H), 3.72 (s, 3H), 1.91 (d,3H).	
622	4-(5-{1-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine	8.79 (dd, 2H), 8.07 (dd,1H), 7.62 (dd, 2H), 7.54 (m, 1H), 7.21 (t, 1H), 5.07 (q, 1H), 3.69 (s, 3H), 1.95 (d, 3H).	418.10
623	4-(5-{1-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyridine	8.79 (dd, 2H), 8.08 (m,1H), 7.57 (m, 3H), 7.22 (t, 1H), 5.21 (q, 1H), 4.08 (q, 2H), 1.97 (d, 3H), 1.35 (t,3H).	

624	2-Chloro-4-[3-(4-cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine	8.83 (m, 2H), 8.65 (m, 1H), 8.05 (t, 1H), 7.92 (t, 1H), 7.76 (t, 2H), 4.82 (2H), 3.31 (m, 1H), 1.23 (m, 2H), 0.86 (m, 2H).	
625	4-{5-[5-(2-Fluoro-5-methyl-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.83 (t, 2H), 7.82 (m, 1H), 7.63 (m, 2H), 7.32 (m, 1H), 7.10 (m, 1H), 4.75 (s, 2H), 3.73 (s, 3H), 2.39 (s, 3H), 1.61 (d, 1H).	
626	4-{4-Ethyl-5-[5-(2-fluoro-5-methyl-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine	8.82 (d, 2H), 7.82 (m, 1H), 7.59 (t, 2H), 7.33 (m, 1H), 7.11 (m, 1H), 4.82 (s, 2H), 4.10 (m, 2H), 2.39 (s, 3H), 1.38 (t, 3H).	397.08
627	4-{4-Cyclopropyl-5-[5-(2-fluoro-5-methyl-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine	8.80 (s, 2H), 7.84 (m, 1H), 7.76 (d, 2H), 7.32 (m, 1H), 7.12 (q, 1H), 4.91 (s, 2H), 3.31 (m, 1H), 2.39 (d, 3H),1.21 (m, 2H), 0.84 (m, 2H).	409.15
628	2-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(2-fluoro-5-methyl-phenyl)-[1,3,4]oxadiazole	7.77 (m, 1H), 7.61 (m, 1H), 7.32 (d, 1H), 7.12 (m, 2H), 6.61 (m, 1H), 4.76 (s, 2H), 4.26 (q, 2H), 2.37 (d, 3H), 1.23 (t, 3H).	

629	2-[4-Ethyl-5-(4-methoxy-phenyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-5-(2-fluoro-5-methyl-phenyl)-[1,3,4]oxadiazole	7.81 (m, 1H), 7.54 (m, 2H), 7.32 (d, 1H), 7.11 (m, 1H), 7.03 (m, 2H), 4.79 (s, 2H), 4.02 (q, 2H), 3.89 (s, 3H), 2.37 (d, 3H), 1.31 (t, 3H).	426.15
630	4-{5-[5-(5-Chloro-2-fluoro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.82 (dd, 2H), 7.91 (dd, 1H), 7.60 (dd, 2H), 7.38 (m, 1H), 7.15 (m, 1H), 6.86 (d, 1H), 4.67 (s, 2H), 4.05 (q, 2H), 1.37 (t, 3H).	417.02
631	4-(5-{1-[5-(5-Chloro-2-fluoro-phenyl)-isoxazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyridine	8.81 (dd, 2H), 7.91 (dd, 1H), 7.59 (dd, 2H), 7.38 (m, 1H), 7.15 (m, 1H), 6.74 (d, 1H), 5.20 (q, 1H), 4.05 (q, 2H), 1.95 (d, 3H), 1.34 (t, 3H).	431.10
632	4-{5-[5-(5-Chloro-2-fluoro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.82 (dd, 2H), 7.91 (dd, 1H), 7.63 (dd, 2H), 7.39 (m, 1H), 7.15 (m, 1H), 6.85 (d, 1H), 4.62 (s, 2H), 3.69 (s, 3H).	403.10
633	4-(5-{1-[5-(5-Chloro-2-fluoro-phenyl)-isoxazol-3-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine	8.81 (dd, 2H), 7.91 (dd, 1H), 7.60 (dd, 2H), 7.38 (m, 1H), 7.15 (m, 1H), 6.72 (d, 1H), 5.06 (q, 1H), 3.64 (s, 3H), 1.93 (d, 3H).	417.10

634	4-{5-[5-(5-Chloro-2-fluoro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-cyclopropyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.80 (dd, 2H), 7.92 (dd, 1H), 7.76 (dd, 2H), 7.38 (m, 1H), 7.15 (m, 1H), 6.95 (d, 1H), 4.71 (s, 2H), 3.27 (m, 1H), 1.18 (m, 2H), 0.82 (m, 2H).	429.10
635	4-(5-{1-[5-(5-Chloro-2-fluoro-phenyl)-isoxazol-3-yl]-ethylsulfanyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine	8.78 (dd, 2H), 7.92 (dd, 1H), 7.76 (dd, 2H), 7.38 (m, 1H), 7.15 (m, 1H), 6.85 (d, 1H), 5.40 (q, 1H), 3.24 (m, 1H),1.98 (d, 3H), 1.88 (m, 2H), 0.80 (m, 2H).	443.20
636	3-[5-(5-Chloro-2-fluoro-phenyl)-isoxazol-3-ylmethylsulfanyl]-4-ethyl-5-furan-2-yl-4H-[1,2,4]triazole	7.90 (dd, 1H), 7.60 (dd, 1H), 7.39 (m, 1H), 7.11 (m, 2H), 6.85 (d, 1H), 6.59 (dd, 1H), 4.62 (s, 2H), 4.20 (q, 2H), 1.38 (t, 3H).	
637	3-{1-[5-(5-Chloro-2-fluoro-phenyl)-isoxazol-3-yl]-ethylsulfanyl}-4-ethyl-5-furan-2-yl-4H-[1,2,4]triazole	7.88 (dd, 1H), 7.59 (dd, 1H), 7.39 (m, 1H), 7.11 (m, 2H), 6.74 (d, 1H), 6.58 (dd, 1H), 5.08 (q, 1H), 4.20 (q, 2H), 1.92 (d, 3H), 1.34 (t, 3H).	
638	4-(5-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine	1.96 (d, 3 H) 3.61 (s, 3 H) 5.10 (q, 1 H) 7.38 (t, 1 H) 7.47 (m, 1 H) 7.54 (m, 2 H) 7.84 (m, 1 H) 7.93 (m, 1 H) 8.74 (d, 2 H)	

639	4-(5-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyridine	8.80 (bs, 2H), 7.99 (m, 1H), 7.90 (m, 1H), 7.58 (d, 2H), 7.51 (m, 1H), 7.46 (t, 1H), 5.31 (q, 1H), 4.06 (q, 2H), 2.04 (d, 3H), 1.31 (t, 3H).	414.10
640	4-(5-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine	8.79 (bs, 2H), 8.03 (m, 1H), 7.94 (d, 1H), 7.76 (d, 2H), 7.51 (m, 1H), 7.45 (t, 1H), 7.54 (q, 1H), 3.25 (m, 1H), 2.06 (d, 3H), 1.19 (m, 2H), 0.81 (m, 2H).	426.07
641	5-(5-Chloro-2-fluoro-phenyl)-3-(5-furan-2-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	8.06 (dd, 1H), 7.60 (d, 1H), 7.55 (m, 1H), 7.22 (t, 1H), 7.09 (d, 1H), 6.58 (m,1H), 4.55 (s, 2H), 3.81 (s, 3H).	
642	5-(5-Chloro-2-fluoro-phenyl)-3-(5-furan-3-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	8.06 (dd, 1H), 7.89 (d, 1H), 7.55 (m, 2H), 7.22 (t, 1H), 6.88 (dd,1H), 4.55 (s, 2H), 3.67 (s, 3H).	
643	4-Chloro-2-[3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-phenol	10.08(s,1H), 7.88(d, 1H), 7.47 (m, 3H), 7.17 (t,1H), 7.06 (d, 1H), 4.68 (s, 2H), 4.14 (q, 2H), 1.38 (t, 3H).	

644	2-Chloro-4-[5-(4-methyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-pyridine	8.83 (d, 2H), 8.60 (m, 1H), 7.94 (m, 1H), 7.85 (m, 1H), 7.62 (m, 2H), 4.82 (s, 2H), 3.75 (s, 3H).	
645	2-Chloro-4-[5-(4-ethyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-pyridine	8.82 (d, 2H), 8.60 (m, 1H), 7.94 (m, 1H), 7.86 (m, 1H), 7.59 (m, 2H), 4.87 (s, 2H), 4.12 (q, 2H), 1.43 (t, 3H).	
646	2-Chloro-4-[5-(4-cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-pyridine	8.81 (d, 2H), 8.60 (m, 1H), 7.96 (m, 1H), 7.86 (m, 1H), 7.75 (m, 2H), 4.92 (s, 2H), 3.32 (m, 1H), 1.21 (m, 2H), 0.87 (q, 2H).	
647	2-Chloro-4-[5-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-pyridine	8.57 (m, 1H), 7.92 (m, 1H), 7.81 (m, 1H), 7.61 (m, 1H), 7.12 (m, 1H), 6.61 (m, 1H), 4.79 (s, 2H), 4.26 (q, 2H), 1.40 (t, 3H).	
648	2-Chloro-4-{5-[4-ethyl-5-(4-methoxy-phenyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,3,4]oxadiazol-2-yl}-pyridine	8.59 (m, 1H), 7.94 (m, 1H), 7.84 (m, 1H), 7.55 (m, 2H), 7.05 (m, 2H), 4.83 (s, 2H), 4.02 (q, 2H), 1.34 (t, 3H).	

649	2-(3-Chloro-phenyl)-5-{1-[5-(4-methoxy-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,3,4]oxadiazole	8.00 (m, 1H), 7.87 (d, 1H), 7.53 (m, 3H), 7.42 (t, 1H), 7.01 (m, 2H), 5.07 (q, 1H), 3.88 (s, 3H), 3.54 (s, 3H), 2.00 (d, 3H).	
650	4-(5-{1-[5-(5-Chloro-2-fluoro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine	8.81 (bs, 2H), 8.01 (m, 1H), 7.63 (d, 2H), 7.50 (m, 1H), 7.18 (m, 1H), 5.17 (q, 1H), 3.69 (s, 3H), 2.02 (d, 3H).	
651	5-(5-Bromo-2-fluoro-phenyl)-3-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	8.20 (m, 1H), 7.65 (m, 1H), 7.60 (s, 1H), 7.13 (m, 2H), 6.56 (m, 1H), 4.64 (s, 2H), 4.25 (q, 2H), 1.38 (t, 3H).	
652	2-(3-Chloro-phenyl)-5-[5-(4-methoxy-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,3,4]oxadiazole	8.02 (d, 1H), 7.90 (d, 1H), 7.50 (m, 4H), 7.03 (d, 2H), 4.71 (s, 2H), 3.88 (s, 3H), 3.61 (s, 3H).	
653	4-{5-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-cyclopropyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.79 (d, 2H), 8.09 (t, 1H), 7.97 (m, 1H), 7.76 (d, 2H), 7.45 (m, 2H), 4.89 (s, 2H), 3.30 (m, 1H), 1.22 (m, 2H), 0.86 (m, 2H).	412.07

654	4-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-cyclopropyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.78 (s, 2H), 8.14 (m, 1H), 8.04 (m, 1H), 7.77 (t, 2H), 7.54 (m, 2H), 4.79 (s, 2H), 3.29 (m, 1H), 1.21 (m, 2H), 0.85 (d, 2H).	
655	4-(5-{1-[5-(2-Fluoro-5-methyl-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine	8.79 (s, 2H), 7.79 (t, 1H), 7.61 (t, 2H), 7.33 (m, 1H), 7.08 (m, 1H), 5.09 (m, 1H), 3.65 (s, 3H), 2.37 (s, 3H), 2.02 (d, 3H).	
656	4-(4-Ethyl-5-{1-[5-(2-fluoro-5-methyl-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4H-[1,2,4]triazol-3-yl)-pyridine	8.81 (m, 2H), 8.23 (m, 1H), 7.79 (d, 2H), 7.32 (m, 1H), 7.09 (m, 1H), 5.28 (m, 1H), 4.07 (m, 2H), 2.37 (s, 3H), 2.04 (d, 3H), 1.24 (m, 3H).	
657	4-(4-Cyclopropyl-5-{1-[5-(2-fluoro-5-methyl-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4H-[1,2,4]triazol-3-yl)-pyridine	8.78 (m, 2H), 7.82 (d, 1H), 7.74 (d, 2H), 7.31 (m, 1H), 7.11 (m, 1H), 5.51 (m, 1H), 3.23 (m, 1H), 2.38 (s, 3H), 2.06 (d, 3H), 1.16 (m, 2H), 0.78 (m, 2H).	

658	4-(4-Cyclopropylmethyl-5-{1-[5-(2-fluoro-5-methyl-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4H-[1,2,4]triazol-3-yl)-pyridine	8.83 (m, 2H), 7.78 (m, 1H), 7.59 (m, 2H), 7.33 (m, 1H), 7.10 (m, 1H), 5.26 (m, 1H), 3.90 (m, 2H), 2.37 (s, 3H), 2.03 (d, 3H), 0.92 (m, 1H), 0.48 (m, 2H), 0.21 (m, 2H).	
659	2-(2-Fluoro-5-methyl-phenyl)-5-{1-[4-methyl-5-(2-methyl-thiazol-4-yl)-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,3,4]oxadiazole	7.98 (s, 1H), 7.75 (m, 1H), 7.31 (m, 1H), 7.08 (m, 1H), 5.03 (q, 1H), 3.85 (s, 3H), 2.75 (s, 3H), 2.35 (s, 3H), 1.98 (d, 3H).	
660	4-(5-{1-[5-(5-Chloro-2-fluoro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyridine	8.80 (m, 2H), 8.01 (m, 1H), 7.58 (m, 2H), 7.49 (m, 1H), 7.19 (m, 1H), 5.32 (q, 1H), 4.08 (q, 2H), 2.04 (d, 3H), 1.35 (t, 3H).	
661	4-(5-{1-[5-(5-Chloro-2-fluoro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine	8.79 (d, 2H), 8.03 (m, 1H), 7.75 (m, 2H), 7.50 (m, 1H), 7.20 (m, 1H), 5.55 (q, 1H), 3.26 (s, 1H), 2.06 (d, 3H), 1.18 (m, 2H), 0.81 (m, 2H).	

662	2-(5-Chloro-2-fluoro-phenyl)-5-[1-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,3,4]oxadiazole	8.97 (m, 1H), 7.59 (m, 1H), 7.47 (m, 1H), 7.17 (m, 1H), 7.12 (m, 1H), 6.59 (m, 1H), 5.18 (q, 1H), 4.21 (q, 2H), 2.00 (d, 3H), 1.33 (t, 3H).	
663	2-(5-Chloro-2-fluoro-phenyl)-5-{1-[4-methyl-5-(2-methyl-thiazol-4-yl)-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,3,4]oxadiazole	7.99 (s, 1H), 7.96 (m, 1H), 7.48 (m, 1H), 7.17 (t, 1H), 7.06 (q, 1H), 3.86 (s, 3H), 2.75 (s, 3H), 1.98 (d, 3H).	
664	4-(4-Cyclopropylmethyl-5-{1-[5-(2-fluoro-5-methyl-phenyl)-isoxazol-3-yl]-ethylsulfanyl}-4H-[1,2,4]triazol-3-yl)-pyridine	8.78 (dd, 2H), 7.71 (dd, 1H), 7.58 (dd, 2H), 7.25 (m, 1H), 7.08 (m, 1H), 6.62 (d, 1H), 5.12 (q, 1H), 3.87 (dd, 2H), 2.40 (s, 3H), 1.94 (d, 3H), 0.90 (m, 1H), 0.49 (m, 2H), 0.19 (m, 2H).	
665	4-(5-{1-[5-(3-Fluoro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine	8.78 (bs, 2H), 7.92 (d, 1H), 7.80 (dd, 1H), 7.60 (d, 2H), 7.50 (m,1H), 7.25 (m, 1H), 5.05 (q, 2H), 3.65 (s, 3H), 1.94 (d, 3H).	

666	4-(4-Cyclopropyl-5-{1-[5-(3-fluoro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4H-[1,2,4]triazol-3-yl)-pyridine	8.76 (d, 2H), 7.95 (d, 1H), 7.85 (dd, 1H), 7.75 (d, 2H), 7.50 (m,1H), 7.25 (m, 1H), 5.45 (q, 2H), 3.20 (m, 1H), 1.98 (d, 3H) 1.22 (m, 2H), 0.88 (m, 2H).	
667	4-(5-{1-[5-(4-Methoxy-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,3,4]oxadiazol-2-yl)-2-methyl-pyridine	8.65 (d, 1H), 7.71 (s, 1H), 7.63 (d, 1H), 7.54 (d, 2H), 7.00 (d, 2H), 5.10 (q, 1H), 3.87 (s, 3H), 3.53 (s, 3H), 2.58 (s, 3H), 2.00 (d, 3H).	
668	4-(5-{1-[4-Ethyl-5-(4-methoxy-phenyl)-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,3,4]oxadiazol-2-yl)-2-methyl-pyridine	8.65 (d, 1H), 7.71 (s, 1H), 7.63 (d, 1H), 7.49 (d, 2H), 7.01 (d, 2H), 5.26 (q, 1H), 3.96 (q, 2H), 3.88 (s, 3H), 2.62 (s, 3H), 2.02 (d, 3H), 1.24 (t, 3H).	
669	4-{5-[1-(4-Ethyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,3,4]oxadiazol-2-yl}-2-methyl-pyridine	8.79 (d, 2H), 8.67 (d, 1H), 7.73 (s, 1H), 7.65 (d, 1H), 7.55 (d, 2H), 5.33 (q, 1H), 4.08 (q, 2H), 2.64 (s, 3H), 2.03 (d, 3H), 1.30 (t, 3H).	

670	4-{5-[1-(4-Cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,3,4]oxadiazol-2-yl}-2-methyl-pyridine	8.77 (d, 2H), 8.68 (d, 1H), 7.72 (m, 4H), 5.55 (q, 1H), 3.24 (m, 1H), 2.64 (s, 3H), 2.04 (d, 3H), 1.16 (m, 2H), 0.81 (m, 2H).	
671	4-{5-[1-(5-Furan-2-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,3,4]oxadiazol-2-yl}-2-methyl-pyridine	8.61 (d, 1H), 7.57 (m, 3H), 7.08 (d, 1H), 6.57 (d, 1H), 5.02 (q, 1H), 3.70 (s, 3H), 1.96 (d, 3H).	
672	2-(3-Chloro-phenyl)-5-{1-[4-methyl-5-(2-methyl-thiazol-4-yl)-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,3,4]oxadiazole	7.99 (s, 1H), 7.94 (m,1H), 7.86 (m, 1H), 7.48 (m, 1H), 7.39 (m, 1H), 5.03 (q, 1H), 3.82 (t, 3H), 2.73 (d, 3H), 1.98 (d, 3H).	
673	3-(5-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine	8.88 (s, 1H), 8.76 (d, 1H), 8.00 (m, 2H), 7.90 (d, 1H), 7.48 (m, 3H), 5.14 (q, 1H), 3.60 (s, 3H), 2.02 (d, 3H).	
674	4-(5-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-2-methyl-pyridine	8.66 (d, 1H), 7.99 (m, 1H), 7.88 (m, 1H), 7.51 (m, 1H), 7.43 (m, 2H), 7.34 (d, 1H), 5.13 (q, 1H), 3.61 (s, 3H), 2.63 (s, 3H), 2.00 (d, 3H).	

675	4-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine	8.68 (dd, 2H), 8.05 (d, 1H), 7.92 (d, 1H), 7.67 (dd, 2H), 7.51 (d, 1H), 7.37 (t, 1H) 5.37 (q, 1H), 3.18 (m, 1H), 1.90 (d, 3H), 1.08 (m, 2H), 0.74 (m, 2H).	
676	5-(3-Chloro-phenyl)-3-{1-[5-(4-methoxy-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,2,4]oxadiazole	8.01 (s, 1H), 7.90 (d, 1H), 7.50 (m, 3H), 7.38 (t, 1H), 6.92 (d, 2H), 4.88 (q, 1H) 3.78 (s, 3H), 3.47 (s, 3H), 1.83 (d, 3H).	
677	4-(5-{1-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine	8.70 (dd, 2H), 8.05 (m, 1H), 7.67 (m, 2H), 7.46 (m, 1H), 7.18 (m, 1H), 5.41 (q, 1H), 3.18 (m, 1H), 1.90 (d, 3H), 1.08 (m, 2H), 0.74 (m, 2H).	
678	5-(5-Chloro-2-fluoro-phenyl)-3-{1-[5-(4-methoxy-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,2,4]oxadiazole	8.05 (m, 1H), 7.56 (m, 3H), 7.21 (t, 1H), 7.00 (m, 3H), 5.01 (q, 1H), 3.85 (s, 3H), 3.56 (s, 3H), 1.90 (d, 3H).	
679	4-[5-(4-Ethyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-2-methyl-pyridine	8.79 (d, 2H), 8.67 (d, 1H), 7.75 (s, 1H), 7.67 (d, 1H), 7.56 (d, 2H), 4.82 (s, 2H), 4.10 (q, 2H), 2.64 (s, 3H), 1.39 (t, 3H).	

680	4-[5-(4-Cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-2-methyl-pyridine	8.78 (d, 3H), 8.68 (d, 1H), 7.74 (m, 4H), 4.90 (s, 2H), 3.30 (m, 1H), 2.65 (s, 3H), 1.21 (m, 2H), 0.84 (m, 2H).	
681	4-{5-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-cyclopropyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.79 (d, 2H), 8.12 (m, 1H), 7.76 (m, 2H), 7.57 (m, 1H), 7.25 (m, 1H), 4.81 (s, 2H), 3.31 (m, 1H), 1.20 (m, 2H), 0.85 (m, 2H).	
682	4-[5-(5-Furan-2-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,3,4]oxadiazol-2-yl]-2-methyl-pyridine	8.66 (d, 1H), 7.72(s, 1H), 7.65 (d, 1H), 7.60 (d, 1H), 7.11 (d, 1H), 6.60(d of d, 1H), 4.70 (s, 2H), 3.80 (s, 3H), 2.64 (s, 3H).	
683	4-(5-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-4-cyclopropylmethyl-4H-[1,2,4]triazol-3-yl)-pyridine	8.79 (bs, 2H), 7.98 (m, 1H), 7.88 (m, 1H), 7.51 (m, 4H), 5.30 (q, 1H), 3.90 (m, 2H), 2.05 (t, 3H), 0.94 (ms, 1H), 0.50 (m, 2H), 0.19 (m, 2H).	
684	4-(5-{1-[5-(4-Fluoro-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,3,4]oxadiazol-2-yl)-2-methyl-pyridine	8.66 (d, 1H), 7.72 (s, 1H), 7.60 (m, 3H), 7.17 (m, 3H), 5.13 (q, 1H), 3.57 (s, 3H), 2.63 (s, 3H), 2.00 (d, 3H).	

685	4-(5-{1-[5-(3-Fluoro-phenyl)-4-methyl-4H-[1,2,4]triazol-3-ylsulfanyl]-ethyl}-[1,3,4]oxadiazol-2-yl)-2-methyl-pyridine	8.65 (d, 1H), 7.72 (s, 1H), 7.66 (d, 1H), 7.48-7.20 (m, 4H), 5.15 (q, 1H), 3.60 (s, 3H), 2.63 (s, 3H), 2.01 (d, 3H).	
686	3-[3-(4-Cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-4-fluoro-benzonitrile	8.77 (dd, 2H), 8.49 (dd,1H), 7.90 (m, 1H), 7.74 (dd, 2H), 7.43 (t, 1H), 4.81 (s, 2H), 3.31 (m, 1H), 1.21 (m, 2H), 0.83 (m, 2H).	
687	4-Chloro-2-[3-(4-cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-phenol	10.15 (bs, 1H), 8.77 (dd, 2H), 7.89 (d,1H), 7.75 (dd, 2H), 7.45 (dd, 1H), 7.06 (d, 1H), 4.79 (s, 2H), 3.29 (m, 1H), 1.21 (m, 2H), 0.83 (m, 2H).	
688	4-{4-Cyclopropyl-5-[5-(3-methoxy-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine	8.77 (dd, 2H), 7.72 (m, 3H), 7.62 (dd, 1H), 7.43 (t, 1H), 7.14 (m, 1H), 4.77 (s, 2H), 3.88 (s, 3H), 3.28 (m, 1H), 1.17 (m, 2H), 0.84 (m, 2H).	
689	4-{4-Cyclopropyl-5-[5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine	8.7 (q, 2H), 7.81 (d, 1H), 7.7 (q, 2H), 7.29 (m, 1H), 7.1 (t, 1H), 4.71 (s, 2H), 3.23 (m, 1H), 2.32 (s, 3H), 1.11 (m, 2H), 0.76 (m, 2H)	

690	4-{4-Cyclopropyl-5-[5-(3-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine	8.67 (m, 2H), 7.82 (m, 1H), 7.72 (m, 1H), 7.66 (m, 1H), 7.42 (m, 1H), 7.21 (m, 1H), 4.68 (s, 1H), 3.23 (m, 1H), 1.11 (m, 2H), 0.75 (m, 2H)	
691	4-[4-Cyclopropyl-5-(5-m-tolyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-4H-[1,2,4]triazol-3-yl]-pyridine	8.69 (q, 2H), 7.85 (m, 2H), 7.67 (q, 2H), 7.32 (m, 2H), 4.69 (s, 2H), 3.2 (m, 1H), 2.35 (s, 3H), 1.11 (m, 2H), 0.76 (m, 2H)	
692	3-[3-(4-Cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzonitrile	8.71 (b s, 2H), 8.36 (m, 1H), 8.28 (d, 1H), 7.83 (d d, 1H), 7.67 (m, 3H), 4.72 (s, 2H), 3.23 (m, 1H), 1.14 (m, 2H), 0.77 (m, 2H)	
693	4-{4-Cyclopropyl-5-[5-(2,5-difluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine	8.75 (t, 2H), 7.79 (m, 2H), 7.26 (m, 2H), 4.78 (s, 2H), 3.28 (m, 1H), 1.14 (m, 2H), 0.82 (m, 2H)	
694	4-{4-Cyclopropyl-5-[1-(5-m-tolyl-[1,2,4]oxadiazol-3-yl)-ethylsulfanyl]-4H-[1,2,4]triazol-3-yl}-pyridine	8.67 (d d, 2H), 7.87 (m, 2H), 7.67 (d d, 2H), 7.33 (m, 2H), 5.36 (q, 1H), 3.15 (m, 1H), 2.36 (s, 3H), 1.92 (d, 3H), 1.07 (m, 2H), 0.72 (m, 2H)	

695	4-(4-Cyclopropyl-5-{1-[5-(3-methoxy-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4H-[1,2,4]triazol-3-yl)-pyridine	8.69 (m, 2H), 7.6 (m, 3H), 7.52 (m, 1H), 7.35 (t, 1H), 7.04 (d d, 1H), 5.35 (q, 1H), 3.81 (s, 3H), 3.15 (m, 1H), 1.91 (d, 3H), 1.11 (m, 2H), 0.7 (m, 2H)	
696	4-{5-[5-(2-Chloro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-cyclopropyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.69 (d, 2H), 7.78 (m, 1H), 7.67 (m, 2H), 7.35 (d, 1H), 7.24 (m, 1H), 4.72 (s, 2H), 3.22 (m, 1H), 2.31 (s, 3H), 1 (m, 2H), 0.76 (m, 2H)	
697	2-[3-(4-Cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-4-methyl-phenol	9.89 (s, 1H), 8.7 (m, 2H), 7.68 (m, 3H), 7.2 (m, 1H), 6.92 (d, 1H), 4.72 (s, 2H), 3.22 (m, 1H), 2.26 (s, 3H), 1.01 (m, 2H), 0.74 (m, 2H)	
698	4-(5-{1-[5-(2-Chloro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine	8.69 (d d, 2H), 7.8 (q, 1H), 7.67 (m, 2H), 7.35 (d, 1H), 7.22 (m, 1H), 5.4 (q, 1H), 3.16 (m, 1H), 2.32 (s, 3H), 1.93 (d, 3H), 1.09 (m, 2H), 0.73 (m, 2H)	

[0863] Example 699

[0864] **{3-[3-(4-Methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-phenyl}-methanol**

[0865] [3-(3-Chloromethyl-[1,2,4]oxadiazol-5-yl)-phenyl]-methanol (32 mg, 0.14

mmol), 4-methyl-5-thiophene-3-yl-4H-[1,2,4]triazole-3-thiol (41 mg, 0.21 mmol) and potassium carbonate (29 mg, 0.21 mmol) was dissolved in anhydrous acetonitrile and refluxed under nitrogen atmosphere for 1 h. The solvent was removed in vacuo and the residue was dissolved in NaHCO3 (aq) and extracted with dichloromethane ('3). The organic phase was dried (MgSO4), filtered and concentrated. The title compound was isolated as an colorless oil (43 mg, 80%) by flash chromatography using 3% methanol in dichloromethane. 1H NMR (CDCl3), δ (ppm): 8.07 (s, 1H), 7.98 (d, 1H), 7.60 (d, 1H), 7.52-7.45 (m, 3H), 7.16 (dd, 1H), 5.29 (s, 2H), 4.75 (s, 2H), 4.50 (s, 2H), 3.71 (s, 1H).

[0866] The following compounds were prepared analogously to Example 699:

Example No.	Name	1H NMR	MS
700	3-[5-(4-Methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-3-yl]-phenol		
701	5-(3-Chloro-phenyl)-3-[4-(tetrahydro-furan-2-ylmethyl)-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole	1.5 (m, 1 H) 1.8 (m, 2 H) 2.0 (m, 1 H) 3.7 (m, 1 H) 3.8 (m, 1 H) 4.1 (s,m, 3 H) 4.5 (dd, 2 H) 7.1 (dd, 1 H) 7.4 (t, 2 H) 7.5 (m, 2 H) 7.9 (dd, 1 H) 8.0 (m, 1 H	460
702	(2-Chloro-phenyl)-{5-[5-(3-chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-isobutyl-4H-[1,2,4]triazol-3-yl}-methanol	0.8 (2 d, 6 H) 2.0 (m, 1 H) 3.5 (dd, 1 H) 3.6 (dd, 1 H) 4.5 (s, 2 H) 6.3 (d, 1 H) 7.3 (m, 3 H) 7.5 (apparent triplett, 1 H) 7.6 (m, 2 H) 8.0 (apparent d, 1 H) 8.1 (m, 1 H)	490

703	5-(2-Fluoro-5-methyl-phenyl)-3-[5-thiophen-2-yl-4-(2,2,2-trifluoro-ethyl)-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole	2.4 (s, 3 H) 4.6 (s, 2 H) 4.8 (q, J=7.7 Hz, 2 H) 7.1 (m, 1 H) 7.2 (m, 1 H) 7.4 (m, 1 H) 7.5 (m, 1 H) 7.6 (m, 1 H) 7.8 (m, 1 H)	455.9

[0867] Example 704

[0868] **3-(2,5-Difluoro-phenyl)-5-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole**

[0869] 5-Chloromethyl-3-(2,5-difluoro-phenyl)-[1,2,4]oxadiazole (23 mg, 0.10 mmol) and 4-ethyl-5-thiophen-2-yl-2,4-dihydro-[1,2,4]triazole-3-thione (23 mg, 0.11 mmol) was dissolved in anhydrous *DMF* (1 ml) and potassium carbonate (21 mg, 0.15 mmol) was added. After stirring for 22 h ethyl acetate was added, the resulting mixture was washed twice with water and once with brine, dried over MgSO4 and evaporated. Flash chromatography using heptane:ethyl acetate 1:1 yielded the title compound (20 mg, 50%). 1H NMR (CDCl3) d (ppm): 7.64 (m, 1H), 7.45 (d, 1H), 7.39 (d, 1H), 7.10 (*m*, 3H), 4.70 (s, 2H), 4.08 (q, 2H), 1.32 (t, 3H).

[0870] The following compounds were prepared analogously to Examples 704:

Example No.	Name	1H NMR	MS
705	5-Furan-3-yl-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	3.71 (s, 3 H) 4.51 (s, 2 H) 6.88 (dd, 1 H) 7.17 (dd, 1 H) 7.48 (dd, 1 H) 7.51 (dd, 1 H) 7.54 (t, 1 H) 8.18 (m, 1 H)	345.92

706	3-(3-Chloro-phenyl)-5-(5-furan-2-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	3.78 (s, 3 H) 4.64 (s, 2 H) 6.57 (dd, 1 H) 7.09 (d, 1 H) 7.38 (t, 1 H) 7.46 (m, 1 H) 7.58 (d, 1 H) 7.91 (d, 1 H) 8.01 (m, 1 H)	373.96
707	3-(3-Chloro-phenyl)-5-(5-furan-3-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	3.63 (s, 3 H) 4.64 (s, 2 H) 6.85 (d, 1 H) 7.39 (t, 1 H) 7.47 (dt, 1 H) 7.56 (t, 1 H) 7.87 (br. s, 1 H) 7.91 (dt, 1 H) 8.01 (t, 1 H)	373.96
708	5-(3-Chloro-phenyl)-3-(5-furan-2-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	3.77 (s, 3 H) 4.50 (s, 2 H) 6.55 (dd, 1 H) 7.07 (d, 1 H) 7.43 (t, 1 H) 7.55 (m, 2 H) 7.95 (dt, 1 H) 8.05 (t, 1 H)	373.96
709	5-(3-Chloro-phenyl)-3-(5-furan-3-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	3.63 (s, 3 H) 4.49 (s, 2 H) 6.84 (br. s, 1 H) 7.43 (t, 1 H) 7.54 (m, 2 H) 7.87 (s, 1 H) 7.94 (d, 1 H) 8.04 (m, 1 H)	373.97
710	4-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyrimidine	4.06 (s, 3 H) 4.63 (s, 2 H) 7.43 (t, 1 H) 7.53 (m, 1 H) 7.95 (d, 1 H) 8.05 (t, 1 H) 8.27 (dd, 1 H) 8.85 (d, 1 H) 9.25 (d, 1 H)	385.97

711	4-{5-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyrimidine	4.06 (s, 3 H) 4.75 (s, 2 H) 7.35 (t, 1 H) 7.42 (ddd, 1 H) 7.88 (dt, 1 H) 7.97 (t, 1 H) 8.24 (dd, 1 H) 8.84 (d, 1 H) 9.23 (d, 1 H)	385.97
712	3-(5-Chloro-2-fluoro-phenyl)-5-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	1.29 (t, 3 H) 4.07 (q, 2 H) 4.68 (s, 2 H) 7.08 (m, 2 H) 7.35 (m, 2 H) 7.44 (dd, 1 H) 7.87 (dd, 1 H)	421.99
713	3-(5-Chloro-2-fluoro-phenyl)-5-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	1.32 (t, 3 H) 4.18 (q, 2 H) 4.71 (s, 2 H) 6.51 (dd, 1 H) 7.02 (dd, 1 H) 7.10 (dd, 1 H) 7.37 (ddd, 1 H) 7.53 (dd, 1 H) 7.91 (dd, 1 H)	406.02
714	5-(5-Chloro-thiophen-2-yl)-3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	1.30 (t, 3 H) 4.09 (q, 2 H) 4.47 (s, 2 H) 6.96 (d, 1 H) 7.11 (dd, 1 H) 7.40 (dd, 1 H) 7.47 (dd, 1 H) 7.60 (d, 1 H)	409.92
715	5-(5-Chloro-thiophen-2-yl)-3-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	1.33 (t, 3 H) 4.21 (q, 2 H) 4.52 (s, 2 H) 6.54 (dd, 1 H) 6.98 (d, 1 H) 7.05 (dd, 1 H) 7.55 (dd, 1 H) 7.62 (d, 1 H)	393.96

716	5-(5-Chloro-thiophen-3-yl)-3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	1.36 (t, 3 H) 4.12 (q, 2 H) 4.58 (s, 2 H) 7.15 (dd, 1 H) 7.43 (m, 2 H) 7.48 (dd, 1 H) 7.94 (d, 1 H)	409.92
717	4-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-ylmethoxy}-phenol	1.30 (t, 3 H) 4.02 (q, 2 H) 4.51 (s, 2 H) 5.07 (s, 2 H) 6.72 (m, 4 H) 7.39 (t, 1 H) 7.49 (m, 1 H) 7.89 (m, 1 H) 7.99 (t, 1 H)	443.9
718	4-{5-[5-(5-Chloro-2-fluoro-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-4-ethyl-4H-[1,2,4]triazol-3-ylmethoxy}-phenol	1.33 (t, 3 H) 4.05 (q, 2 H) 4.70 (s, 2 H) 5.11 (s, 2 H) 6.74 (m, 4 H) 7.13 (t, 1 H) 7.44 (m, 1 H) 7.93 (dd, 1 H)	461.9
719	3-(2,5-Difluoro-phenyl)-5-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	7.75 (m, 1H), 7.64 (d, 1H), 7.23 (m, 2H), 7.16 (d, 1H), 6.63 (dd, 1H), 4.80 (s, 2H), 4.29 (q, 2H), 1.43 (t, 3H)	389.9
720	3-(2,5-Difluoro-phenyl)-5-(5-furan-2-yl-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	8.17 (dd, 1H), 7.87 (m, 1H), 7.74 (m, 2H), 7.33 (dd, 1H), 6.95 (dd, 1H), 5.01 (s, 2H), 3.96 (s, 3H)	375.8

721	4-(5-{1-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine	8.74 (d, 2 H), 7.97 (s, 1 H), 7.87 (m, 1 H), 7.56 (d, 2 H), 7.44 (m, 1 H), 7.36 (apparent t, 1 H), 5.06 (q, 1 H), 3.58 (s, 3 H), 1.96 (d, 3 H).	400
722	4-{5-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-cyclopropyl-4H-[1,2,4]triazol-3-yl}-pyrimidine	0.90 (m, 2 H), 1.22 (m, 2 H), 3.49 (m, 1 H), 4.81 (s, 2 H), 7.26 (t, 1 H), 7.53 (m, 1 H), 8.11 (m, 2 H), 8.88 (d, 1 H) 9.33 (s, 1 H)	430.1
723	2-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-5-methoxy-pyrimidine	1.32 (t, 3 H), 1.94 (d, 3 H), 4.00 (s, 3H), 4.50 (m, 2 H), 5.20 (q, 1 H), 7.46 (t, 1 H), 7.56 (m, 1 H), 7.99 (d, 1 H), 8.10 (t, 1 H), 8.56 (d, 2 H).	444.1
724	2-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyrimidine	1.34 (t, 3 H), 1.94 (d, 3 H), 4.50 (m, 2 H), 5.26 (q, 1 H), 7.36 (t, 1 H), 7.46 (t, 1 H), 7.57 (d, 1 H), 7.99 (m, 1 H), 8.10 (m, 1 H), 8.92 (d, 2 H).	414

725	4-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-2-methoxy-pyridine	1.32 (t, 3 H), 1.97 (d, 3 H), 3.99 (s, 3H), 4.06 (m, 2 H), 5.19(q, 1 H), 6.98 (bs, 1 H), 7.16 (m, 1 H), 7.47 (t, 1 H), 7.58 (m, 1 H), 7.98 (dt, 1 H), 8.10 (m, 1 H) 8.31 (d, 1 H).	443.1
726	5-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-2-methoxy-pyridine	1.30 (t, 3 H), 1.96 (d, 3 H), 3.99(m, 2H), 4.00 (s, 3 H), 5.16 (q, 1 H), 6.87 (d, 1 H), 7.47 (t, 1 H), 7.58 (m, 1 H), 7.86 (dd, 1 H), 8.00 (d, 1 H), 8.11 (t, 1 H) 8.40 (d, 1 H).	443
727	2-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-5-methoxy-pyridine	1.30 (t, 3 H), 1.93 (d, 3 H), 3.92 (s, 3 H), 4.52 (m, 2 H), 5.13 (q, 1 H), 7.32 (dd, 1 H), 7.46 (t, 1 H), 7.56 (m, 1 H), 7.99 (dt, 1 H), 8.10 (t, 1 H), 8.25 (d, 1 H) 8.30 (d, 1 H).	443.1
728	3-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-6-methoxy-pyridazine	1.38 (t, 3 H), 1.96 (d, 3 H), 4.20 (s, 3 H), 4.61 (m, 2 H), 5.20 (q, 1 H), 7.12 (d, 1 H), 7.46 (t, 1 H), 7.56 (t, 1 H), 8.00 (d, 1 H), 8.10 (s, 1 H), 8.40 (d, 1 H)	444

729	3-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine	0.77 (m, 2 H), 1.14 (m, 2 H), 1.99 (d, 3 H), 3.22 (m, 1 H), 5.44 (q, 1 H), 7.45 (m, 2 H), 7.58 (d, 1 H), 8.02 (d, 1 H), 8.15 (m, 2 H), 8.72 (d, 1 H) 9.05 (s, 1 H).	
730	4-{5-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine	3.69 (s, 3 H) 4.73 (s, 2 H) 7.39 (t, 1 H) 7.47 (m, 1 H) 7.60 (m, 2 H) 7.92 (m, 1 H) 8.02 (t, 1 H) 8.79 (m, 2 H)	384.91

[0871] Example 731

[0872] **5-(3-Chloro-phenyl)-3-(5-furan-2-yl-4-isobutyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole**

[0873] The title compound was synthesized according to the method described by Graybill et al. Tetrahedron lett. 2002 43, 5305-5309 from furan-2-carboxylic acid hydrazide (55.2 mg, 0.44 mmol), 1-isothiocyanato-2-methyl-propane (47ml, 0.38 mmol) and 3-chloromethyl-5-(3-chloro-phenyl)-[1,2,4]oxadiazole (45.0 mg, 0.20 mmol) with P-BEMP (136 mg, 0.30 mmol) as base. Purification by flash chromatography (33-66% EtOAc in heptane) gave the product as an oil (12.7 mg, 15.6%).1H NMR ($CDCl_3$) d (ppm): 8.08 (s, 1 H), 7.97 (d, 1H), 7.55 (d, 2H), 7.45 (t, 1H), 7.10 (d, 1H), 6.56 (d, 1H), 4.62 (s, 2H), 4.01 (d, 2H), 2.03 (m, 1H), 0.86 (d, 6H).

[0874] General: Thiophene-2-carbohydrazide (1.5 equiv) and an isothiocyanate (1.3 equiv) were dissolved in DMF (1 ml). 2-tert-Butylimino-2-diethylamino-1,3-dimethyl-perhydro-1,3,2-diazaphosporine (1 equiv) on polystyrene was added and the reactions were shaken on a Bohdan miniblock at ambient temperature for 1 h and then for one additional h at 45 °C. The resin was washed with dioxane:water 1:1 several times. The ring closure was carried out at 85 °C for 48 h in dioxane:water 1:1 on the miniblock. The resin was washed with acetonitrile (2´2ml). The 3-(chloromethyl)-5-

(3-chlorophenyl)-1,2,4-oxadiazole was added to the reaction and shaken in acetonitrile at 50 °C for 2h. The product was filtrated and purified on MS-directed prep-HPLC, gradient 0-100% acetonitrile over 15 min.

[0875] The following compounds were prepared analogously to Example 731:

Example No.	Name	1H NMR	MS
732	5-(3-Chloro-phenyl)-3-[4-(3-methylsulfanyl-propyl)-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole		464.0
733	5-(3-Chloro-phenyl)-3-(4-hexyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole		460.0
734	5-(3-Chloro-phenyl)-3-(4-cyclopropylmethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole		430.0
735	5-(3-Chloro-phenyl)-3-[4-(3-fluoro-benzyl)-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole		484.0
736	5-(3-Chloro-phenyl)-3-[4-(3-methyl-benzyl)-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole		480.0
737	5-(3-Chloro-phenyl)-3-[4-(2-methyl-butyl)-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole		446.0

738	5-(3-Chloro-phenyl)-3-[4-(3-methyl-butyl)-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole		446.0
739	5-(3-Chloro-phenyl)-3-[4-(2-fluoro-benzyl)-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole		484.0

[0876] Example 740

[0877] **5-(3-Chloro-phenyl)-3-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-yloxymethyl)-[1,2,4]oxadiazole**

[0878] [5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-methanol (28.0 mg, 0.13 mmol), 4-ethyl-3-methanesulfonyl-5-thiophen-2-yl-4H-[1,2,4]triazole (35.2 mg, 0.13 mmol) and cesium carbonate (130 mg) were dissolved in dimethylformamide and stirred under argon at ambient temperatures for 46 h. After evaporation to dryness the crude was chromatographed on 12 g silica, heptane/ethyl acetate 4/1 to 2/1. Collection of the appropriate fractions gave after evaporation to dryness and drying in vacuo the title compound (17.0 mg, 33%). 1H NMR ($CDCl_3$), δ (ppm): 8.13 (m, 1H), 8.02 (m, 1H), 7.58 (m, 1H), 7.47 (m, 2H), 7.40 (dd, 1H), 7.14 (dd, 1H), 5.74 (s, 2H), 4.04 (q, 2H), 1.38 (t, 3H).

[0879] The following compounds were prepared analogously to Example 740:

Example No.	Name	1H NMR	MS
741	4-{5-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethoxy]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.92 (s broad, 2 H), 8.12 (apparent dd, 1 H), 7.78 (s, 1 H), 7.56 (s broad, 2 H), 7.25 (apparent t, 1 H), 5.79 (s, 2 H), 3.66 (s, 3 H).	388

742	4-(5-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethoxy}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine	8.82 (s broad, 2 H), 8.07-7.94 (m, 2 H), 7.69 (s broad, 2 H), 7.47 (m, 2 H), 6.47 (q, 1 H), 3.63 (s, 3 H), 2.02 (d, 3 H).	384.1
743	4-(5-{1-[3-(3-Chloro-phenyl)-isoxazol-5-yl]-ethoxy}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine	1.92 (d, 3 H), 3.57 (s, 3 H), 6.36 (q, 1 H), 6.74 (s, 1 H), 7.39 (m, 2 H), 7.60 (m, 2 H), 7.66 (m, 1 H), 7.78 (m, 1 H), 8.75 (m, 2 H)	383.1
744	3-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethoxy}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine		

[0880] The following compounds were prepared analogously to Example 740 with the exception that sodium hydride was employed as the base and the reaction was heated at 80°C:

745	4-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethoxy]-4-cyclopropyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.77 (d, 2H), 8.17 (s, 1H), 8.05 (d, 1H), 7.79 (d, 2H), 7.62 (dd, 1H), 7.52 (t, 1H), 5.79 (s, 2H), 3.25 (m, 1H), 1.14 (d, 2H), 0.89 (m, 2H)	

746	4-{5-[5-(3-Chloro-phenyl)-isoxazol-3-ylmethoxy]-4-cyclopropyl-4H-[1,2,4]triazol-3-yl}-pyridine	8.77 (d, 2H), 7.79 (m, 3H), 7.7 (m, 1H), 7.44 (m, 2H), 6.84 (s, 1H), 5.71 (s, 2H), 3.21 (m, 1H), 1.13 (d, 2H), 0.82 (m, 2H)	

[0881] Example 747

[0882] **5-(2-Methoxy-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole**

[0883] HBTU (171 mg, 0.45 mmol) and HOBT (8 mg, 0.06 mmol) were added to a solution of 2-methoxy benzoic acid (68 mg, 0.45 mmol) and DIPEA (192 ml , 1.11 mmol) in DMF (3 ml). After 10 min N-hydroxy-2-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-acetamidine (100 mg, 0.37 mmol) was added. The reaction mixture was stirred at RT for 7 h and then at 110 °C over night. After cooling the reaction mixture was diluted with water and extracted with CH_2Cl_2. The organic phase was dried and concentrated. Flash chromatography (heptane/EtOAc 1:2) afforded 1.9 mg (11%) of the desired product.

1H NMR ($CDCl_3$), d (ppm): 7.99 (m, 1H), 7.53 (m, 1H), 7.50 (m, 1H), 7.47 (m, 1H), 7.16 (m, 1H), 7.04 (m, 2H), 4.52 (s, 2H), 3.94 (s, 3H), 3.71 (s, 3H).

[0884] The following compounds were prepared analogously to Example 747:

Example No.	Name	1H NMR	MS
748	5-Furan-2-yl-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole	3.72 (s, 3 H) 4.52 (s, 2 H) 6.61 (dd, 1 H) 7.16 (dd, 1 H) 7.30 (dd, 1 H) 7.47 (dd, 1 H) 7.50 (dd, 1 H) 7.67 (dd, 1 H)	345.92

749	3-[3-(4-Methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-benzoic acid methyl ester		414.0
750	5-(2-Fluoro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole		374.0
751	5-(2,5-Difluoro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole		392.0
752	3-(4-Methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(3-vinyl-phenyl)-[1,2,4]oxadiazole		382.1
753	5-(3-Difluoromethoxy-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole		422.0
754	5-(4-Methoxy-thiophen-3-yl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole		392.0
755	5-(2-Chloro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole		390.0
756	5-(4-Fluoro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole		374.0

[0885] Example 757

[0886] 3-(3-Chloro-phenyl)-5-[1-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,2,4]oxadiazole

[0887] DMF was added to a mixture of 2-(4-Methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-propionic acid (50 mg, 0.186 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDCI) (35.7 mg, 0.186 mmol), 1-hydroxybenzotriazole hydrate (HOBT) (28.5 mg, 0.186 mmol) and 3-chloro-N-hydroxy-benzamidine (29.3 mg, 0.172 mmol) at room temperature and stirred overnight. The reaction mixture was diluted with ethyl acetate (75 ml), washed with water 3 times, once with 1.0 M HCl (30 ml), saturated $NaHCO_3$ (30 ml) and saturated brine (30 ml), dried over anhydrous sodium sulfate, filtered and concentrated in vacuo. DMF (1 ml) was added to the residue and the resulting solution was heated at 135°C for 3 h to effect cyclization to oxadiazole. After cooling the reaction mixture was diluted with ethyl acetate (75 ml), washed with water 3 times, once with 1.0 M HCl (30 ml), saturated $NaHCO_3$ (30 ml) and saturated brine (30 ml), dried over anhydrous sodium sulfate, filtered and concentrated in vacuo. The title compound (46.5 mg, 66.9%) was purified by SPE chromatography on silica gel using 50 ml 40%, 150 ml 50% ethyl acetate in hexanes. 1H NMR ($CDCl_3$), δ (ppm): 8.03 (s, 1H), 7.92 (m, 1H), 7.47 (m, 4H), 7.18 (dd, 1H), 4.99 (q, 1H), 3.64 (s, 3H), 1.97 (d, 3H).

[0888] The following compounds were prepared analogously to Example 757:

Example No.	Name	1H NMR	MS
758	3-(5-{1-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine	8.88 (d, 1H), 8.76 (dd, 1H), 8.03 (m, 2H), 7.93 (d, 1H), 7.74 (m, 3H), 5.09 (m, 1H), 3.58 (s, 3H), 2.00 (d, 3H)	

[0889] The following compounds were prepared analogously to Example 10:

Example No.	Name

759	5-(1-Chloro-ethyl)-3-(3-chloro-phenyl)-[1,2,4]oxadiazole
	3-(1-Chloro-ethyl)-5-m-tolyl-[1,2,4]oxadiazole
761	3-(1-Chloro-ethyl)-5-(3-methoxy-phenyl)-[1,2,4]oxadiazole
762	3-(1-Chloro-ethyl)-5-(2-chloro-5-methyl-phenyl)-[1,2,4]oxadiazole
763	3-(1-Chloro-ethyl)-5-(2,5-difluoro-phenyl)-[1,2,4]oxadiazole
764	3-(1-Chloro-ethyl)-5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazole
765	3-[3-(1-Chloro-ethyl)-[1,2,4]oxadiazol-5-yl]-benzonitrile

[0890] The following compounds were prepared analogously to Example 40:

Example No.	Name	1H NMR	MS
766	4-(5-{1-[5-(2-Chloro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine	8.74 (d, 2H), 7.79 (s, 1H), 7.57 (d d, 2H), 7.38 (d, 1H), 7.25 (d, 1H), 5 (q, 1H), 3.62 (s, 3H), 2.33 (s, 3H), 1.92 (d, 3H)	
767	4-(5-{1-[5-(2,5-Difluoro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine	8.67 (d, 2H), 7.7 (m, 1H), 7.57 (d d, 2H), 7.2 (m, 2H), 5 (q, 1H), 3.61 (s, 3H), 1.87 (d, 3H)	

768	4-(5-{1-[5-(2-Fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine	8.77 (d, 2H), 7.85 (m, 1H), 7.61 (m, 2H), 7.38 (m, 1H), 7.06 (t, 1H), 5.02 (q, 1H), 3.66 (s, 3H), 2.37 (s, 3H), 1.94 (d, 3H)	
769	4-(4-Cyclopropyl-5-{1-[5-(2-fluoro-5-methyl-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4H-[1,2,4]triazol-3-yl)-pyridine	8.75 (d, 2H), 7.9 (m, 1H), 7.74 (m, 2H), 7.38 (m, 1H), 7.13 (m, 1H), 5.45 (q, 1H), 3.24 (m, 1H), 2.39 (s, 3H), 2 (d, 3H), 1.15 (m, 2H), 0.79 (m, 2H)	
770	3-{3-[1-(4-Methyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,2,4]oxadiazol-5-yl}-benzonitrile	8.76 (d d, 2H), 8.4 (s, 1H), 8.32 (d, 1H), 7.87 (d, 1H), 7.65 (t, 1H), 7.59 (m, 2H), 5.07 (q, 1H), 3.67 (s, 3H), 2.59 (s, 2H), 1.91 (d, 3H)	
771	3-{3-[1-(4-Cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-ylsulfanyl)-ethyl]-[1,2,4]oxadiazol-5-yl}-benzonitrile	8.77 (m, 2H), 8.42 (d, 1H), 8.38 (m, 1H), 7.9 (m, 1H), 7.71 (m, 3H), 5.49 (q, 1H), 3.25 (m, 1H), 2 (d, 3H), 1.17 (m, 2H), 0.81 (m, 2H)	
772	3-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethylsulfanyl}-5-pyridin-4-yl-[1,2,4]triazol-4-ylamine	8.77 (br s, 2H), 8.18 (d, 2H), 7.98 (s, 1H), 7.87 (d, 1H), 7.52 (d, 1H), 7.44 (t, 1H), 5.66 (s, 2H), 4.88 (q, 1H), 1.98 (d, 3H)	

[0891] The following compounds were prepared analogously to Example 316:

Example No.	Name
773	3-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-2-methyl-propionic acid hydrazide
774	Rac-3-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-butyric acid hydrazide

[0892] The following compounds were prepared analogously to Example 318:

Example No.	Name
775	2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-cyclopropanecarboxylic acid hydrazide

[0893] Example 776

[0894] **3-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-2,2-dimethyl-propionic acid hydrazide**

[0895] 3,3-Dimethyl-dihydro-furan-2,5-dione (6.4g) was heated at 50oC in ethanol (150 mL) overnight. The solvent was removed *in vacuo* and the residue triturated with hexane to yield 2,2-Dimethyl-succinic acid 4-ethyl ester (4.66g) which was used without further purification. t-Butanol (7.5 mL) was added to a mixture of 2,2-Dimethyl-succinic acid 4-ethyl ester (2.74g, 15.7mmol) in dichloromethane (62 mL) containing magnesium sulfate (7.5 g) and conc. sulfuric acid (0.85 mL) and the mixture was stirred at room temperature overnight. Saturated sodium bicarbonate solution was added and the product was extracted into dichloromethane, washed with brine solution, dried and concentrated to yield the diested as a colorloess oil (1.89 g). The ethyl ester was hydrolyzed by trating the crude sample with potassium hydroxide (2.75g) in a mixture of ethanol (50 mL) and water (25 mL) at room temperatire for 2h. The reaction was acidified using 1N HCl (aq) and extracted into ether, dried and concentrated to yield 2,2-Dimethyl-succinic acid 1-tert-butyl ester (1.4g). This acid was treated under the conditions of Example 320 (step 1) to yield 3-[3-(3-Chloro-

phenyl)-[1,2,4]oxadiazol-5-yl]-2,2-dimethyl-propionic acid tert-butyl ester (1.9g). This t-Bu ester was deprotected using formic acid (19 mL) at 50°C for 20 min. The crude product was concentrated and triturated with a mixture of ether and hexane to yield 3-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-2,2-dimethyl-propionic acid (1.12g). To a solution of 3-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-2,2-dimethyl-propionic acid (561 mg, 2 mmol) and triethylamine (1.1 mL, 8 mmol) in THF (9 ml), isobutyl chloroformate (0.31 mL, 2.4 mmol) was added dropwise at -78 °C. After being stirred for 1h, hydrazine hydrate (1 mL, 11 mmol) was added. The reaction mixture was stirred at room temperature for 1 h and concentrated. A small amount of ice was added to quence any excess reagent and precipitate the product, which was collected by filtration to give 482 mg of the title compound.

[0896] The following compounds were prepared analogously to Example 320:

Example No.	Name
777	(S)-{1-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-2-hydrazinocarbonyl-ethyl}-carbamic acid tert-butyl ester

[0897] Example 778

[0898] **3-(3-Chloro-phenyl)-5-[2-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-yl)-ethyl]-[1,2,4]oxadiazole**

[0899] Step 1: 3-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propionic acid (ethoxy-thiophen-2-yl-methylene)-hydrazide: 3-[3-(3-chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propionic acid hydrazide (266.69 mg, 1 mmol) was mixed with thiophene-2-carboximidic acid ethyl ester (191.6 mg, 1mmol) in ethanol (6 ml) and stirred at room temperature overnight. The reaction was quenched with water, extracted with ethyl acetate, dried and concentrated in vacuo. The crude product was triturated with hexane to yield 3-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propionic acid (ethoxy-thiophen-2-yl-methylene)-hydrazide as a white solid (305 mg, 75%). 1H-NMR($CDCl_3$) d(ppm): 8.99 (ws, 1H), 8.09 (s, 1H), 7.98 (d, 1H), 7.41(m, 4H), 7.08 (dd, 1H), 4.27 (q, 2H), 3.34 (m, 4H) and 1.41 (t, 3H). Step 2: 3-(3-Chloro-phenyl)-5-[2-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-yl)-ethyl]-

[1,2,4]oxadiazole: 3-[3-(3-chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propionic acid (ethoxy-thiophen-2-yl-methylene)-hydrazide (81 mg, 0.2 mmol) was mixed with 2M methylamine (0.3 ml in THF) in ethanol (2 ml) at 70~80 °C overnight. The reaction mixture was concentrated with silica gel and purified by column chromatography with 0.5~2.0% methanol in ethyl acetate to give 54 mg (72.5 %) of 3-(3-chloro-phenyl)-5-[2-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-yl)-ethyl]-[1,2,4]oxadiazole. 1H-NMR($CDCl_3$) d (ppm): 8.08 (s, 1H), 7.97 (d, 1H), 7.41 (m, 4H), 7.20 (dd, 1H), 3.80 (s, 3H), 3.68 (dd, 2H), 3.38 (dd, 2H).

[0900] The following compounds were prepared analogously to Example 778:

Example No.	Name	1H NMR	MS
779	3-(3-Chloro-phenyl)-5-[2-(4-ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-yl)-ethyl]-[1,2,4]oxadiazole	8.08 (s, 1H), 7.97 (d, 1H), 7.47(m, 4H), 7.20 (dd, 1H), 4.20 (q, 2H), 3.72 (dd, 2H), 3.38 (dd, 2H) and 1.47 (t, 3H)	
780	5-(3-Chloro-phenyl)-3-(5-furan-2-yl-4-methyl-4H-[1,2,4]triazol-3-ylmethyl)-[1,2,4]oxadiazole	8.11 (s, 1H), 8.01 (d, 1H), 7.61(s, 1H), 7.58 (d, 1H), 7.48 (t, 1H), 7.11 (d, 1H), 6.59 (m, 1H), 4.48 (s, 2H) and 3.92 (s, 3H)	
781	2-(3-Chloro-phenyl)-5-[2-(5-furan-2-yl-4-methyl-4H-[1,2,4]triazol-3-yl)-ethyl]-[1,3,4]oxadiazole	8.04 (s, 1H), 7.93 (d, 1H), 7.60(s, 1H), 7.52 (d, 1H), 7.46 (t, 1H), 7.06 (d, 1H), 6.59 (m, 1H), 3.87 (s, 3H), 3.65 (t, 2H) and 3.38 (t, 2H)	

782	2-(3-Chloro-phenyl)-5-[2-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-yl)-ethyl]-[1,3,4]oxadiazole	8.05 (s, 1H), 7.94 (d, 1H), 7.60(s, 1H), 7.52 (d, 1H), 7.47 (t, 1H), 7.10 (d, 1H), 6.59 (m, 1H), 4.30 (q, 2H), 3.67 (t, 2H), 3.39 (t, 2H) and 1.43 (t, 3H)	
783	2-(3-Chloro-phenyl)-5-[2-(4-cyclopropyl-5-furan-2-yl-4H-[1,2,4]triazol-3-yl)-ethyl]-[1,3,4]oxadiazole	8.05 (s, 1H), 7.94 (d, 1H), 7.63 (s, 1H), 7.52 (d, 1H), 7.46 (t, 1H), 7.01 (d, 1H), 6.58 (m, 1H), 3.67 (dd, 2H), 3.51 (t, 2H), 3.33 (m, 1H) 1.25 (m, 2H) and 0.93 (m, 2H)	383.12

[0901] Example 784

[0902] **4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-ethyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine**

[0903] Step 1: Isonicotinic acid {4-[3-(3-chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-1-ethoxy-butylidene}-hydrazide: 3-[3-(3-chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propionimidic acid ethyl ester hydrochloride (473.3, 1.5 mmol) was mixed with isonicotinic acid hydrazide (205.7 mg, 1.5 mmol) in ethanol (8 ml) at 60 °C for an h and then at room temperature for 2 h. The reaction mixture was diluted with dichloromethane and washed with water. The organic layer was dried, concentrated with vacuum and the residue was triturated with ether to give 490 mg (78.9 %) of isonicotinic acid {4-[3-(3-chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-1-ethoxy-butylidene}-hydrazide as white solid.

[0904] Step 2: 4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-ethyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine (47.1 mg, 82 %) as white solid was obtained from isonicotinic acid {4-[3-(3-chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-1-ethoxy-

butylidene}-hydrazide (60 mg, 0.15 mmol) reacted with 2M methylamine (0.45 ml, 0.9 mmol) in ethanol (1 ml) at 60 °C overnight. 1H-NMR($CDCl_3$) d(ppm): 8.77 (d, 2H), 8.02 (s, 1H), 7.91 (d, 1H), 7.58(d, 2H), 7.42 (m, 2H), 3.76 (s, 3H), 3.66 (t, 2H) and 3.38 (t, 2H).

[0905] The following compounds were prepared analogously to Example 784:

Example No.	Name	1H NMR	MS
785	4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-ethyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyridine	8.79 (d, 2H), 8.05 (s, 1H), 7.94 (d, 1H), 7:58(d, 2H), 7.43 (m, 2H), 4.16 (q, 2H), 3.72 (t, 2H), 3.40 (t, 2H) and 1.44 (t, 3H)	
786	4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-ethyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine	8.77 (d, 2H), 8.05 (s, 1H), 7.93 (d, 1H), 7.73(d, 2H), 7.44 (m, 2H), 3.72(t, 3H), 3.51 (t, 2H), 3.38 (m, 1H), 1.23 (m, 2H) and 0.79 (m, 2H)	

[0906] Example 787

[0907] **4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine**

[0908] Step 1: N-Cyclopropyl-isonicotinamide: Isonicotinic acid ethyl ester (3.0 g, 20 mmol) was mixed with cyclopropylamine (2 ml) at 120 °C in a sealed vial for 40 h. The reaction mixture was triturated with ether to give 1.62 g (50 %) of N-cyclopropyl-isonicotinamide as off-white solid. 1H-NMR($CDCl_3$) d (ppm): 8.73 (d, 2H), 7.60 (d, 2H) and 6.55 (w, 1H), 2.92 (m, 1H), 0.90 (m, 2H) and 0.66 (m, 2H). Step 2: N-Cyclopropyl-isonicotinimidoyl chloride hydrochloride: N-Cyclopropyl-isonicotinamide (1.62 g, 10 mmol) was reacted with SOCl2 (12 g, 100 mol) at 80 °C

overnight. The reaction mixture was concentrated and triturated with dichloromethane to give 1.3 g (64%) of N-cyclopropyl-isonicotinimidoyl chloride hydrochloride as yellow solid. Step 3: 4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine: (R)-3-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-butyric acid hydrazide (56 mg, 0.2 mmol) was mixed with N-cyclopropyl-isonicotinimidoyl chloride hydrochloride (40.6 mg, 0.2 mmol) and K_2CO_3 (60 mg, 0.43 mmol) in DMF (1 ml) at 100 °C for 3 h. The reaction mixture was dilute with dichloromethane and then washed with water. The organic layer was concentrated and purified with 5~6 % methanol in ethyl acetate to give 32 mg (39%) of the title comound. 1H-NMR($CDCl_3$) d (ppm): 8.78 (d, 2H), 8.05 (s, 1H), 7.96(d, 1H), 7.73(d, 2H), 7.45(m, 2H), 4.15 (q, 1H), 3.64 (dd, 1H), 3.31 (m, 2H), 1.68 (d, 3H), 1.25 (m, 2H) and 0.79 (m, 2H).

[0909] The following compounds were prepared analogously to Example 787: It should be noted that some reactions provided 1,3,4-oxadiazole cyclization products with loss of the methylamino or cycopropylamino group instead of or as well as the triazole product.

Example No.	Name	1H NMR	MS
788	4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-2-methyl-propyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine	8.74 (d, 2H), 8.04 (s, 1H), 7.94 (d, 1H), 7.67 (d, 2H), 7.43 (m, 2H), 3.48(s, 2H), 3.09 (m, 1H), 1.75 (s, 6H), 1.16 (m, 2H) and 0.68 (m, 2H)	

789	4-(5-{2-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-propyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine	8.76 (w, 2H), 8.03 (s, 1H), 7.92 (d, 1H), 7.72(d, 2H), 7.44 (m, 2H), 4.13(m, 1H), 3.72 (dd, 1H), 3.43 (m, 1H), 3.27 (dd, 1H), 1.66 (d, 3H), 1.25 (m, 2H) and 0.79 (m, 2H)	
790	4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-1-methyl-ethyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine	8.78 (d, 2H), 8.01 (s, 1H), 7.91 (d, 1H), 7.73 (d, 2H), 7.49 (d, 1H), 7.42 (t, 1H), 3.99 (m, 1H), 3.83 (dd, 1H), 3.48 (m, 1H), 3.39 (m, 1H), 1.61 (d, 3H), 1.25 (m, 2H), 0.98 (m, 1H), 0.74 (m, 1H)	
791	cis-4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-cyclopropyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine	8.73 (d, 2H), 7.88 (s, 1H), 7.78 (d, 1H), 7.65 (d, 2H), 7.41 (d, 1H), 7.34 (t, 1H), 3.20 (m, 1H), 2.89 (m, 2H), 2.54 (dd, 1H), 2.00 (td, 1H), 1.20 (m, 2H), 0.83 (m, 2H)	
792	4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-1,1-dimethyl-ethyl}-[1,3,4]oxadiazol-2-yl)-pyridine	8.82 (m, 2H), 7.98 (s, 1H), 7.90 (m, 3H), 7.47 (d, 1H), 7.39 (t, 1H), 3.51 (s, 2H), 1.70 (s, 6H)	

793	4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-2-methyl-propyl}-[1,3,4]oxadiazol-2-yl)-pyridine	8.76 (d, 2H), 8.07 (s, 1H), 7.97 (d, 1H), 7.77 (d, 2H), 7.49 (dd, 1H), 7.43 (t, 1H), 3.53 (s, 2H), 1.69 (s, 6H)	
794	4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-1-methyl-ethyl}-[1,3,4]oxadiazol-2-yl)-pyridine	8.82 (d, 2H), 8.05 (m, 1H), 7.95 (d, 1H), 7.91 (d, 2H), 7.50 (dd, 1H), 7.42 (t, 1H), 3.94 (dd, 1H), 3.67 (dd, 1H), 3.41 (dd, 1H), 1.66 (d, 3H)	
795	4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-cyclopropyl}-[1,3,4]oxadiazol-2-yl)-pyridine	8.77 (d, 2H), 7.81 (m, 4H), 7.42 (d, 1H), 7.32 (t, 1H), 3.07 (q, 1H), 2.99 (q, 1H), 2.41 (q, 1H), 2.08 (td, 1H)	
796	4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-cyclopropyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine	8.76 (d, 2H), 7.85 (m, 1H), 7.77 (d, 1H), 7.55 (d, 2H), 7.44 (dd, 1H), 7.34 (t, 1H), 3.70 (s, 3H), 2.89 (m, 1H), 2.72 (m, 1H), 2.51 (q, 1H), 2.02 (dt, 1H)	
797	4-(5-{2-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-propyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine	8.79 (d, 2H), 8.02 (s, 1H), 7.93 (d, 1H), 7.59 (d, 2H), 7.53 (d, 1H), 7.46 (t, 1H), 4.03 (m, 1H), 3.80 (s, 3H), 3.52 (m, 1H), 3.23 (dd, 1H), 1.66 (d, 3H)	

798	4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propyl}-[1,3,4]oxadiazol-2-yl)-pyridine	8.81 (d, 2H), 8.07 (s, 1H), 7.97 (d, 1H), 7.87 (d, 2H), 7.50 (d, 1H), 7.43 (t, 1H), 3.91 (q, 1H), 3.66 (dd, 1H), 3.44 (dd, 1H), 1.65 (d, 3H)	
799	4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine	8.80 (d, 2H), 8.05 (s, 1H), 7.95 (d, 1H), 7.61 (d, 2H), 7.51 (d, 1H), 7.45 (t, 1H), 4.07 (q, 1H), 3.75 (s, 3H), 3.48 (dd, 1H), 3.23 (dd, 1H), 1.68 (d, 3H)	
800	4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine	8.78 (d, 2H), 8.05 (s, 1H), 7.96 (d, 1H), 7.74 (d, 2H), 7.50 (dd, 1H), 7.46 (t, 1H), 4.15 (q, 1H), 3.64 (dd, 1H), 3.31 (m, 2H), 1.67 (d, 3H), 1.25 (m, 2H), 0.81 (m, 2H)	
801	(S)-[1-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-2-(4-cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-yl)-ethyl]-carbamic acid tert-butyl ester		

[0910] Example 802

[0911] (S)-1-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-2-(4-cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-yl)-ethylamine

[0912] (S)-[1-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-2-(4-cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-yl)-ethyl]-carbamic acid tert-butyl ester (135 mg) was mixed with 96 % formic acid (1.3 mL) and heated at 50 °C for 1 h. The reaction mixture was concentrated *in vacuo*. The residue was quenched with saturated sodium bicarbonate and extracted with ethyl acetate. The organic layer was dried with sodium sulfate and concentrated. Purification was performed by flash column silica gel chromatography with 2-3% (2 M ammonia methanol) in dichloromethane to give 106 mg of the title compound as an off-white solid. 1H NMR ($CDCl_3$):d ppm 8.73 (d, 2H), 8.03 (s, 1H), 7.93 (d, 1H), 7.69 (d, 2H), 7.46 (d, 1H), 7.42 (t, 1H), 5.02 (dd, 1H), 3.61 (dd, 1H), 3.49 (dd, 1H), 3.35 (m, 1H), 2.47 (br s, 2H), 1.20 (m, 2H), 0.75 (m, 2H)

[0913] Example 803

[0914] (S)-[1-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-2-(4-cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-yl)-ethyl]-dimethyl-amine

[0915] Sodium cyanoborohydride (0.1 mL, 1M in THF) was added to a solution of (S)-1-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-2-(4-cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-yl)-ethylamine (30 mg) in methanol (0.8 mL) containing 96% formic acid (0.1 mL) and 37% formalin solution (0.1 mL). The residue was quenched with water and extracted with ethyl acetate. The organic layer was dried with sodium sulfate and concentrated. Purification was performed by flash column silica gel chromatography with 3% (2 M ammonia methanol) in dichloromethane to give 22 mg of the title compound.

1H NMR ($CDCl_3$):d ppm 8.76 (d, 2H), 8.06 (s, 1H), 7.97 (d, 1H), 7.73 (d, 2H), 7.47 (d, 1H), 7.45 (t, 1H), 5.00 (dd, 1H), 3.76 (dd, 1H), 3.51 (dd, 1H), 3.42 (m, 1H), 2.45 (br s, 6H), 1.26 (m, 2H), 0.88 (m, 1H), 0.79 (m, 1H)

[0916] Example 804

[0917] 8-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethyl]-3-pyridin-4-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridine

[0918] 37 mg (0.25 mmol) Me3OBF4 was added to a solution of 60 mg (0.21 mmol) 3-[5-(3-chloro -phenyl)-[1,2,4]oxadiazol-3-ylmethyl]-piperidin-2-one in 2 ml

CH_2Cl_2. The mixture was stirred overnight at room temperature. The reaction mixture was diluted with CH_2Cl_2, washed with NaHCO3 (sat), dried and concentrated. The residue was dissolved in 3 ml EtOH and 22 mg (0.16 mmol) isonicotinic hydrazide was added. The solution was heated with microwaves at 120 °C for 10 min. The reaction mixture was cooled and the volatiles were removed under reduced pressure. The crude product was purified by preparative HPLC to afford 17 mg (20%) of the desired product. 1H NMR ($CDCl_3$):d ppm 1.75 (m, 1 H) 1.99 (m, 1 H) 2.21 (m, 2 H) 3.16 (dd, 1 H) 3.73 (m, 1 H) 3.85 (dd, 1 H) 4.07 (m, 1 H) 4.19 (m, 1 H) 7.47 (t, 1 H) 7.56 (m, 1 H) 7.67 (m, 2 H) 8.01 (m, 1 H) 8.11 m, 1 H) 8.76 (d, 2 H).

[0919] The following compounds were prepared analogously to Example 804:

Example No.	Name	1H NMR	MS
805	8-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethyl]-3-thiophen-2-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridine	1.69 (m, 1 H) 1.99 (m, 1 H) 2.18 (m, 2 H) 3.11 (m, 1 H) 3.67 (m, 1 H) 3.87 (m, 1 H) 4.02 (m, 1 H) 4.24 (m, 1 H) 7.15 (m, 1 H) 7.47 (m, 3 H) 7.56 (m, 1 H) 8.01 (d, J=7.83 Hz, 1 H) 8.12 (d, J=1.77 Hz, 1 H)	
806	8-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethyl]-3-pyridin-4-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridine	1.76 (m, 1 H) 2.00 (m, 1 H) 2.21 (m, 2 H) 3.22 (dd, , 1 H) 3.74 (m, 1 H) 3.87 (dd, 1 H) 4.09 (m, 1 H) 4.19 (m, 1 H) 7.23 (m, 1 H) 7.53 (m, 1 H) 7.68 (m, 2 H) 8.10 (dd, 1 H) 8.77 (m, 2 H)	

[0920] Example 807

[0921] 5-(5-Bromo-4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-3-(3-chloro-phenyl)-[1,2,4]oxadiazole

[0922] 3-(3-Chloro-phenyl)-5-(4-methyl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole was mixed with 30 ml of chloroform/pyridine(25/1) at room temperature. Then bromine in chloroform (0.5 ml) was added dropwise and the reaction mixture was heated at 70 °C overnight. The reaction mixture was diluted with chloroform and washed with saturated NH_4Cl twice and the organic layer was dried with sodium sulfate, concentrated, the residue was triturated with diethyl ether to give the title compound (1.5 g, 57.5 %, yellow solid). 1H-NMR($CDCl_3$) d(ppm): 8.05 (s, 1H), 7.94 (d, 1H), 7.47(d, 1H), 7.43 (t, 1H), 4.66 (s, 2H) and 3.59 (s, 3H).

[0923] Example 808

[0924] 3-[3-(4-Methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-phenylamine

[0925] To {3-[3-(4-Methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)[1,2,4] oxadiazole 5-yl-phenyl}-carbamic acid tert-butyl ester (88.0 mg, 0.19 mmol) in dichloromethane (3 ml) at 0°C added TFA (1.5 ml) and allowed to stir for 1 h. The reaction mixture was warmed to room temperature and the solvent was removed under vacuum. Dichloromethane was added to the resulting residue and the mixture was cooled to 0°C and saturated sodium bicarbonate was added to the stirring solution until turning basic (pH ~ 8). The mixture was then transferred to a separatory funnel and the product was extracted with dichloromethane, dried using anhydrous sodium sulfate, and concentrated in vacuo. The resulting residue was titurated with ether and 61.1mg (87%) of 3-[3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-phenylamine was isolated (light yellow solid). 1H NMR (DMSO-d6) d (ppm): 7.81 (d, 1H), 7.64 (d, 1H), 7.23 (m, 4H), 6.84 (d, 1H), 5.57 (s, 2H), 4.50 (s, 2H), 3.72 (s, 3H).

[0926] The following compounds were prepared analogously to Example 98:

Example No.	Name	1H NMR	MS

809	5-(3-Chloro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazole-3-sulfonylmethyl)-[1,2,4]oxadiazole		423.01
810	5-(3-Chloro-phenyl)-3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazole-3-sulfinylmethyl)-[1,2,4]oxadiazole		

[0927] The following compounds were prepared analogously to Example 93:

Example No.	Name	1H NMR	MS
811	2-Methyl-6-[3-(4-methyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-pyridine		

[0928] Example 812

[0929] **4-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-pyridin-2-ol**

[0930] HBr (1 ml) and HOAc (1 ml) were added to 4-(5-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethylsulfanyl}-4-ethyl-4H-[1,2,4]triazol-3-yl)-2-methoxy-pyridine (9 mg, 0.02 mmol) and the reaction was stirred at 80 °C on. Saturated $NaHCO_3$ (aq) was added to the reaction and the mixture was extracted three times with dichloromethane. The combined organic phases were dried and concentrated to give the title compound (8.5 mg, 99 %). 1H NMR ($CDCl_3$), δ (ppm): 1.37 (t, 3 H), 1.96 (d, 3 H), 4.10 (q, 2 H), 5.23 (q, 1 H), 6.80 (m, 2 H), 7.49 (t, 2 H), 7.59 (m, 1 H), 7.99 (d, 1 H), 8.11 (s, 1 H).

Example 813

[0931] 4-(5-{2-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-propyl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine

[0932] 84 microl (0.21 mmol, 2.5 M) n-BuLi was added dropwise to a solution of 37 mg (0.21 mmol) 4-(4,5-dimethyl-4H-[1,2,4]triazol-3-yl)-pyridine in 2.1 ml THF at

0°C. After 20 min a solution of 60 mg (0.21 mmol) 3-(1-bromo-ethyl)-5-(3-chloro-phenyl)-[1,2,4]oxadiazole was added dropwise. The reaction mixture was allowed to reach room temperature and stirred over night. NH_4Cl(sat) was added and the mixture was extracted twice with EtOAc. The organic phase was dried and concentrated. Flashchromatography (CH_2Cl_2/MeOH 20:1) afforded 7.7 mg (10%) of the desired product. 1H NMR ($CDCl_3$), d (ppm): 1.57 (d, 3 H) 3.16 (m, 1 H) 3.38 (m, 1 H) 3.71 (s, 3 H) 3.84 (d, 1 H) 7.46 (t, 1 H) 7.55 (m, 1 H) 7.58 (m, 2 H) 7.98 (m, 1 H) 8.10 (t, 1 H) 8.77 (d, 2 H)

[0933] Example 814

[0934] [5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethyl]-methyl-(4-methyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-yl)-amine

[0935] 10 mg (0.4 mmol) NaH was added to a solution of 38 mg (0.2 mmol) methyl-(4-methyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-yl)-amine in 3 ml DMF under an atmosphere of nitrogen. After 10 min a solution of 50 mg (0.22 mmol) 3-chloromethyl-5-(3-chloro-phenyl)-[1,2,4]oxadiazole in 2 ml DMF was added. After stirring for 45 min NH_4Cl(sat) was added and the mixture was extracted twice with $CHCl_3$. The organic phase was dried and concentrated. Flashchromatography (CH_2Cl_2/MeOH 20:1) afforded 41 mg (54%) of the desired product. 1H NMR ($CDCl_3$), d (ppm): 3.07 (s, 3 H) 3.71 (s, 3 H) 4.56 (s, 2 H) 7.45 (m, 1 H) 7.55 (m, 1 H) 7.62 (d, 2 H) 7.98 (d, 1 H) 8.09 (m, 1 H) 8.73 (d, 2 H).

Example 815

[0936] 8-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethyl]-3-pyridin-4-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrimidine

[0937] 32 mg (1.31 mmol) NaH was added to a solution of 193 mg (0.96 mmol) 3-pyridin-4-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrimidine in 10 ml DMF at room temperature. After 10 min 200 mg (0.87mmol) 5-(3-chloro-phenyl)-3-chloromethyl-[1,2,4]oxadiazole was added to the reaction mixture. The reaction mixture was stirred at room temperature over night. The reaction mixture was diluted with NH_4Cl(sat) and extracted twice with EtOAc. The combined organic phases were

washed with water, dried and concentrated. Flashchromatography (CH_2Cl_2/MeOH 20:1) afforded 111 mg (32%) of a white solid. 1H NMR ($CDCl_3$), d (ppm): 2.24 (m, 2 H) 3.57 (m, 2 H) 4.15 (m, 2 H) 5.01 (s, 2 H) 7.46 (t, 1 H) 7.56 (d, 1 H) 7.62 (d, 2 H) 7.99 (d, 1 H) 8.10 (s, 1 H) 8.70 (d, 2 H).

[0938] The following compounds were prepared analogously to Example 815:

Example No.	Name	1H NMR	MS
816	8-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethyl]-3-pyridin-4-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrimidine		
817	8-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-ylmethyl]-3-pyridin-4-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrimidine		
818	8-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethyl}-3-pyridin-4-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrimidine	1.81 (d, 3 H) 2.19 (m, 2 H) 3.47 (m, 2 H) 4.12 (m, 2 H) 6.07 (q, 1 H) 7.42 (m, 1 H) 7.49 (m, 1 H) 7.61 (m, 2 H) 7.91 (m, 1 H) 8.00 (m, 1 H) 8.70 (m, 2 H)	
819	8-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethyl]-3-furan-2-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrimidine	2.23 (m, 2 H) 3.50 (m, 2 H) 4.20 (m, 2 H) 4.97 (s, 2 H) 6.49 (m, 1 H) 6.89 (d, 1 H) 7.19 (t, 1 H) 7.48 (m, 1 H) 7.51 /m, 1 H) 8.06 (m, 1 H)	

820	8-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethyl}-3-pyridin-4-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrimidine	1.74 (d, 3 H) 2.17 (m, 2 H) 3.45 (m, 2 H) 4.10 (m, 2 H) 5.96 (m, 1 H) 7.44 (t, 1 H) 7.53 (m, 1 H) 7.59 (m, 2 H) 7.97 (m, 1 H) 8.08 (m, 1 H) 8.67 (d, 2 H)	

[0939] Example 821

[0940] **3-(4-Ethyl-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-5-(1H-pyrrol-3-yl)-[1,2,4]oxadiazole**

[0941] 3-Chloromethyl-5-[1-(toluene-4-sulfonyl)-1H-pyrrol-3-yl]-[1,2,4]oxadiazole (50 mg) and potassium hydroxide (50 mg) was heated for two h in methanol (5 ml). The mixture was diluted with ethyl acetate (10 ml), washed with water and brine, dried over $MgSO_4$, filtered and concentrated. The title compound was isolated in 57% yield by flash chromatography on silica gel using 40% ethyl acetate in heptane. 1H NMR ($CDCl_3$) d (ppm): 9.8 (s, 1H), 7.5 (m, 2H), 7.4 (d, 1H), 7.2 (dd, 1H), 6.8 (m, 1H), 6.7 (d, 1H), 4.5 (s, 2H), 4.1 (q, 2H), 1.4 (t, 3H).

[0942] Example 822

[0943] **4-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine 1-oxide**

[0944] 4-{5-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-4-methyl-4H-[1,2,4]triazol-3-yl}-pyridine and wet 57%-86% MCPBA (52.4 mg, 0.20-0.30 mmol) were dissolved in dichloromethane (4 ml) and stirred for 16 h. The reaction mixture was purified via reversed phase preparative LC to give the title compound (7.5 mg, 8%). 1H NMR ($CDCl_3$), δ (ppm): 8.33 (d, 2 H), 8.06 (m, 1 H), 7.96 (m, 1 H), 7.67 (d, 2 H), 7.57 (m, 1 H), 7.46 (apparent t, 1 H), 4.60 (s, 2 H), 3.71 (s, 3 H).

[0945] Example 823

[0946] **5-(3-Chloro-phenyl)-3-(2-furan-2-yl-3-methyl-3H-imidazol-4-**

ylsulfanylmethyl)-[1,2,4]oxadiazole

[0947] 2-Furan-2-yl-3-methyl-3,5-dihydro-imidazol-4-one (described in Takeuchi, H., Hagiwara, S., Eguchi, S., Tetrahedron (1989) 6375-6386) (50 mg, 0.30 mmol) was dissolved in dioxane (3 ml) and Lawesson reagent (136 mg, 0.34 mmol) was added. The reaction mixture was heated to reflux over night and then allowed to room temperature at which time DIPEA (212 ml, 1.22 mmol) and 3-chloromethyl-5-(3-chloro-phenyl)-[1,2,4]oxadiazole (140 mg, 0.61 mmol) was added. The resulting mixture was heated to reflux for 5h and then kept at room temperature over night. Ethyl acetate was added and the reaction mixture was washed with water followed by brine. The organic phase was dried over $MgSO_4$ and evaporated. The title compound (13 mg, 11%) was obtained by flash chromatography using 1% methanol in chloroform. 1H NMR (CD_3OD) d (ppm): 7.96 (m, 1 H), 7.90 (m, 1H), 7.60 (dd, 1H), 7.57 (ddd, 1H), 7.46 (t, 1H), 7.09 (s, 1H), 6.86 (dd, 1H), 6.52 (dd, 1H), 3.95 (s, 2H), 3.74 (s, 3H).

[0948] Example 824

[0949] **5-(5-Chloro-2-fluoro-phenyl)-3-[4-(2-fluoro-ethyl)-5-thiophen-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl]-[1,2,4]oxadiazole**

[0950] To a cooled (-15 °C) solution of 2-{3-[5-(5-chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-5-thiophen-2-yl-[1,2,4]triazol-4-yl}-ethanol (46 mg, 0.11 mmol) in anhydrous THF (15 ml) was dropwise added DAST (32 ml, 0.24 mmol). The mixture was stirred at room temperature for 1.5 h and was then quenched with MeOH (1 ml). The solvent was removed under reduced pressure and the residue was partitioned between brine and EtOAc. The aqueous layer was extracted with EtOAc (2 x 20 ml). The combined organic layers were washed with brine (10 ml), dried ($MgSO_4$) and concentrated under reduced pressure. Purification by flash chromatography (EtOAc:heptane 2:1) and preparative HPLC afforded the title compound as a white solid (11 mg, 22%). 1H NMR ($CDCl_3$) d (ppm): 8.05 (dd, 1H), 7.52 (m, 3H), 7.20 (m, 1H), 7.16 (m, 1H), 4.75 (t, 1H), 4.63 (m, 3H), 4.45 (m, 2H).

[0951] Example 825

[0952] 5-(5-Chloro-thiophen-3-yl)-3-(4-ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazole

[0953] The title compound was prepared according to method for 2-[5-(3-Methoxy-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1H-benzoimidazole, with the exception of using molar equivalent cesium carbonate instead of potassium carbonate as the base, from 1-[5-(5-chloro-thiophen-3-yl)-[1,2,4]oxadiazol-3-ylmethoxy]-1H-benzotriazole (32.3 mg, 0.097 mmol) and 4-ethyl-5-furan-2-yl-2,4-dihydro-[1,2,4]triazole-3-thione (23 mg) by using 50% EtOAc in n-heptane as chromatography eluent to yield 21 mg. 1H NMR ($CDCl_3$) d (ppm): 7.95 (d, 1H), 7.57 (dd, 1H), 7.44 (d, 1H), 7.07 (dd, 1H), 6.56 (dd, 1H), 4.56 (s, 2H), 4.22 (q, 2H), 1.35 (t, 3H).

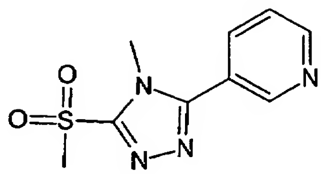
[0954] Example 826

[0955] 3-[3-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-4-hydroxy-benzonitrile

[0956] The title compound was prepared using the general procedure of Rogers et al., Tetrahedron Letters (2002) 43: 3585-3587. To a stirring solution of 3-[3-(4-Ethyl-5-furan-2-yl-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-[1,2,4]oxadiazol-5-yl]-4-fluoro-benzonitrile (20mg, 0.050 mmol), 2-(methylsulfonyl-ethanol) (9.38 mg, 0.075 mmol), and DMF (0.05 M) at 0 °C was added NaH (5.8 mg, 0.150 mmol). Stirred for 20 min and removed the ice bath. Stirred an additional 20 min while warming to room temperature. The reaction mixture was quenched with 1 N HCl solution and partitioned between ethyl acetate and brine. The organic layer was dried (Na_2SO_4), filtered and concentrated to dryness. The crude organics were purified by flash column chromatography using ethyl acetate followed by 5% methanol in ethyl acetate to give the title compound (8.1 mg, 41%, white solid). 1H NMR ($CDCl_3$), δ (ppm): 8.25 (m, 1H), 7.75 (m, 1H), 7.60 (s, 1H), 7.18 (m, 2H), 6.60 (m, 1H), 4.64 (s, 2H), 4.25 (q, 2H), 1.38 (t, 3H).

[0957] Example 827

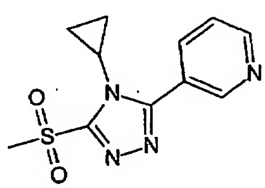
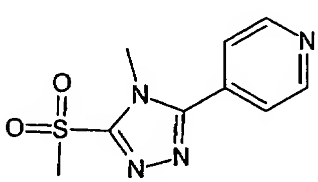
[0958] 3-[4-methyl-5-(methylsulfonyl)-4*H*-1,2,4-triazol-3-yl]pyridine

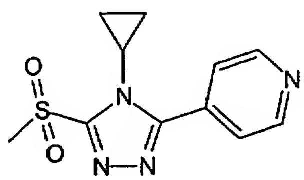


[0959]

[0960] $KMnO_4$ (5g, 32 mmol) was added to a solution of 3-[4-methyl-5-(methylthio)-4H-1,2,4-triazol-3-yl]pyridine (6.0g, 29 mmol) in H_2O (40 mL) and acetic acid (100 mL). After 1 h stirring at rt the reaction was basified with aq. NaOH (4M). $CHCl_3$ was added and the mixture was filtrated through celite. The layers were separated and the water phase was washed with $CHCl_3$. The combined organic phase was dried and concentrated to give 3.67 g (53 %) of the title compound. ^1H NMR: 3.59 (s, 3H) 3.99 (s, 3H) 7.52 (m, 1H) 8.02 (dt, 1H) 8.83 (dd, 1H) 8.91 (m, 1H)

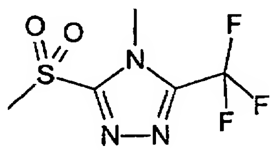
[0961] The following examples were synthesized in a manner analogous to that for 3-[4-methyl-5-(methylsulfonyl)-4*H*-1,2,4-triazol-3-yl]pyridine.

Structure	Name	^{1}H-NMR	Example No.
	3-[4-cyclopropyl-5-(methylsulfonyl)-4*H*-1,2,4-triazol-3-yl]pyridine	0.98 (m, 2H) 1.26 (m, 2H) 3.61 (s, 3H) 3.68 (m, 1H)	828
	4-[4-methyl-5-(methylsulfonyl)-4H-1,2,4-triazol-3-yl]pyridine	(DMSO-D6): 3.6 (s, 3 H) 3.9 (s, 3 H) 7.8 (s, 2 H) 8.8 (s, 2 H)	829

	4-(4-Cyclopropyl-5-methanesulfonyl-4H-1,2,4-triazol-3-yl)-pyridine	8.86 (d, 2H), 7.77 (d , 2H), 3.64 (m, 1H), 3.63 (s, 3H), 1.25 (m, 2H), 1.01 (m, 2H).	**830**

[0962] Example 831

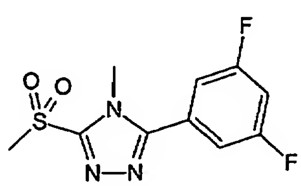
[0963] 4-methyl-3-(methylsulfonyl)-5-(trifluoromethyl)-4*H*-1,2,4-triazole

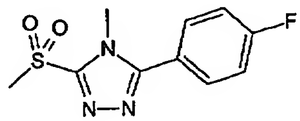


[0964]

[0965] To 4-methyl-3-(methylthio)-5-(trifluoromethyl)-4H-1,2,4-triazole (4.15 g, 21. 0 mmol) in DCM (150 ml) at 0°C was added mCPBA (57-86%, 15.1 g, 52.6 mmol) in portions. After stirring at r.t. o.n. DCM (150 ml) was added. The resulting mixture was washed with sat. aq. $NaHCO_3$, sat. aq. $Na_2S_2O_3$ and brine, dried and evaporated to afford 4.4 g (91%) of the title compound. MS (M^+-1) = 228.

[0966] . The following examples were synthesized in a manner analogous to that for 4-methyl-3-(methylsulfonyl)-5-(trifluoromethyl)-4*H*-1,2,4-triazole.

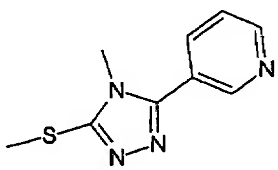
Structure	Name	Analytical data	Example No.
	3-(3,5-difluorophenyl)-4-methyl-5-(methylsulfonyl)-4*H*-1,2,4-triazole	^{1}H-NMR (DMSO-D6): 3.60 (s, 3 H) 3.89 (s, 3 H) 7.56 (s, 3 H) MS (M+1) 242	832

	3-(4-fluorophenyl)-4-methyl-5-(methylsulfonyl)-4*H*-1,2,4-triazole	MS (M^++1) 256	833

[0967] Preparation of Intermediate Compounds

[0968] Example 834

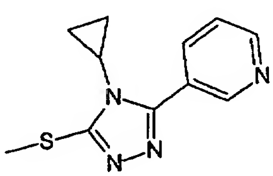
[0969] 3-[4-methyl-5-(methylthio)-4*H*-1,2,4-triazol-3-yl]pyridine

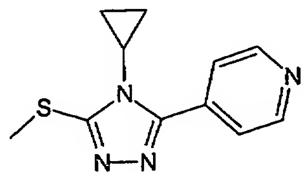
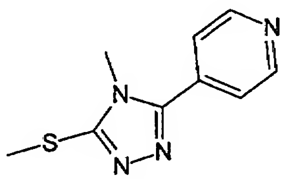
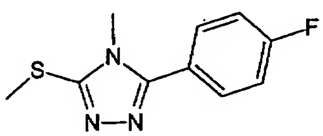


[0970]

[0971] MeI (2 mL, 32 mmol) in EtOH (10 mL) was added to a mixture of 4-methyl-5-pyridin-3-yl-2,4-dihydro-3H-1,2,4-triazole-3-thione in 1 M NaOH (70 mL, 70 mmol). After 1 h stirring at rt, DCM was added and the layers were separated. The water phase was washed with DCM and the combined organic phases were dried and concentrated to give 6.5g (98 %) of the title compound. ^{1}H NMR: 2.76 (s, 3H) 3.59 (s, 3H) 7.43 (m, 1H) 7.99 (m, 1H) 8.71 (m, 1H) 8.86 (m, 1H)

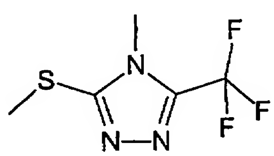
[0972] The following examples were synthesized in a manner analogous to that for 3-[4-methyl-5-(methylthio)-4*H*-1,2,4-triazol-3-yl]pyridine

Structure	Name	Analytical data	Example No.
	3-[4-cyclopropyl-5-(methylthio)-4*H*-1,2,4-triazol-3-yl]pyridine	LC-MS (M^++1): 233	835

	4-(4-Cyclopropyl-5-methylsulfanyl-4H-1,2,4-triazol-3-yl)-pyridine	[1]H NMR: 8.77 (d, 2H), 7.75 (m , 2H), 3.23 (m, 1H), 2.82 (s, 3H), 1.17 (m, 2H), 0.80 (m, 2H).	**836**
	4-[4-methyl-5-(methylthio)-4H-1,2,4-triazol-3-yl]pyridine	[1]H NMR (DMSO-D6): 2.7 (s, 3 H) 3.6 (s, 3 H) 7.7 (m, 2 H) 8.8 (d, 2 H)	**837**
	3-(4-fluorophenyl)-4-methyl-5-(methylthio)-4*H*-1,2,4-triazole	Used directly in the next step towards 3-(4-fluorophenyl)-4-methyl-5-(methylsulfonyl)-4*H*-1,2,4-triazole.	**838**

[0973] Example 839

[0974] 4-methyl-3-(methylthio)-5-(trifluoromethyl)-4*H*-1,2,4-triazole

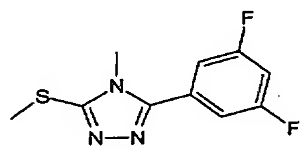


[0975]

[0976] 4-Methylthiosemicarbazid (10.0 g, 95.09 mmol) in TFA (46.7 ml) was heated to reflux o.n.. Excess TFA was removed via evaporation. The residue was dissolved in aq. 1M NaOH (100 ml), followed by dropwise addition of CH_3I (4.47 ml, 71.17 mmol) in EtOH (22 ml). The resulting mixture was stirred o.n. Partial evaporation of the solvent induced crystallization. After dilution with H_2O the solid was collected via filtration and gave after drying the title compound (5.2 g, 28%). MS (M^++1) 198

[0977] Example 840

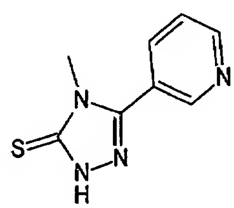
[0978] 3-(3,5-difluorophenyl)-4-methyl-5-(methylthio)-4*H*-1,2,4-triazole

[0979] 

[0980] The title compound was obtained as a byproduct in the synthesis of 5-(3,5-difluorophenyl)-N,4-dimethyl-4H-1,2,4-triazol-3-amine. ^{1}H NMR (DMSO-D6): 2.66 (s, 3 H) 3.60 (s, 3 H) 7.43 - 7.52 (m, 3 H). MS (M^++1) 242.

[0981] Example 841

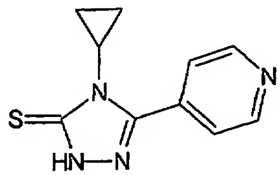
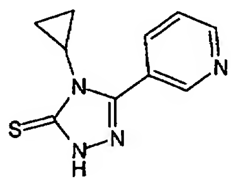
[0982] 4-methyl-5-pyridin-3-yl-2,4-dihydro-3H-1,2,4-triazole-3-thione

[0983] 

[0984] Nicotinohydrazide (10 g, 73 mmol) and methyl isothiocyanate (5.6 g, 76 mmol) were mixed in 2-propanol (150 ml) and heated to 70 °C o.n. The reaction was cooled to r.t. and evaporated to dryness. H_2O (180 mL) and $NaHCO_3$ (12.8 g, 152 mmol) were added to the residue and the mixture was refluxed o.n. The reaction mixture was cooled to rt, acidified with concentrated hydrochloric acid and the title compound, 13.1 g (93%), was collected by filtration. LC-MS (M^++1): 193

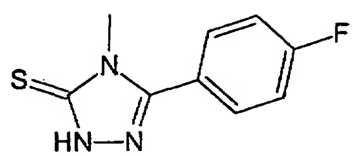
[0985] The following examples were synthesized in a manner analogous to that for 4-methyl-5-pyridin-3-yl-2,4-dihydro-3H-1,2,4-triazole-3-thione

Structure	Name	Analytical data	Example No.

	4-cyclopropyl-5-pyridin-4-yl-2,4-dihydro-3*H*-1,2,4-triazole-3-thione	^{1}H-NMR: 0.63 (m, 2 H) 1.00 (m, 2 H) 3.25 (m, 1 H) 7.75 (d, 2 H) 8.74 (m, 2 H)	**842**
	4-cyclopropyl-5-pyridin-3-yl-2,4-dihydro-3*H*-1,2,4-triazole-3-thione	LC-MS (M^++1): 219	**843**

[0986] Example 844

[0987] 5-(4-fluorophenyl)-4-methyl-2,4-dihydro-3*H*-1,2,4-triazole-3-thione

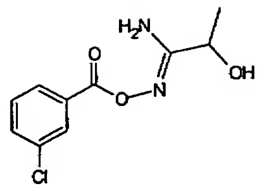


[0988]

[0989] To 4-methylthiosemicarbazid (4.24g, 40.30 mmol) in pyridine (50 ml) was added dropwise 4-fluorobenzoyl chloride (4.9 ml, 40. 00 mmol) and the resulting mixture was stirred at r.t. o.n.. The pyridine was removed by evaporation and the residue was heated in aq. sat. $NaHCO_3$ at reflux o.n.. After cooling to r.t., the product was collected by filtration, washed with water and dried under vacuum to give 3.22 g (38%) which was used in the next step without further purification. ^{1}H NMR: 3.9 (m, 3 H) 6.98 (t, 2 H) 7.92 (m, 2 H).

[0990] Example 845

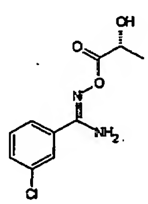
[0991] N'-[(3-chlorobenzoyl)oxy]-2-hydroxypropanimidamide

[0992] 

[0993] 6.45 g crude N',2-dihydroxypropanimidamide was cooled on an ice-bath with 23.5 mL DEA in THF (200 mL). To this slurry 21.94 g 3-chlorobenzoyl chloride was added. The mixture was warmed to r.t. and stirred for 2 h. Addition of Et_2O (200 mL), washing with sat. aq. NH_4Cl and re-extraction of the aq. layer gave after combining and concentration of the org. layers followed by drying in vacuo 27.24 g of crude title compound, which was used directly in the next step for 1-[5-(3-chlorophenyl)-[1,2,4]oxadiazol-3-yl]ethanol. LC-MS (M^{+}+1): 243

[0994] Example 846

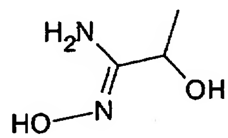
[0995] 3-chloro-N'-{[(2R)-2-hydroxypropanoyl]oxy}benzenecarboximidamide

[0996] 

[0997] 3.82 g (22.4 mmol) of 3-chloro-N'-hydroxybenzenecarboximidamide and 2.00 g (22.2 mmol) of (R)-lactic acid were dissolved under Ar at 0°C in DCM (50mL) and DMF (15mL). After 5 min 3.4 mL (33.2 mmol) DIC and 3.50 g (25.9 mmol) HOBt were added. After 15 min the mixture was warmed to r.t. and stirred for additional 3 h, followed by filtration and washing with DCM. The filtrate was evaporated *in vacuo* to near dryness, taken up in EA and washed with aq. $NaHCO_3$, followed by water and finally 2 M aq. citric acid. The EA layer was filtered over a mixture of Na_2SO_4 and silica. Flash chromatography (Hep/EA=4/1 to 2/1 to 1/2) gave an oil which was triturated with Et_2O to yield after drying 4 g (75%) of the title compound. ^{1}H NMR: 7.69 (t, 1 H), 7.55 - 7.59 (m, 1 H), 7.44 - 7.49 (m, 1 H), 7.36 (t, 1 H), 5.10 (s, 2 H), 4.50 (q, 1 H), 1.54 (d, 3 H)

[0998] Example 847

[0999] N',2-dihydroxypropanimidamide

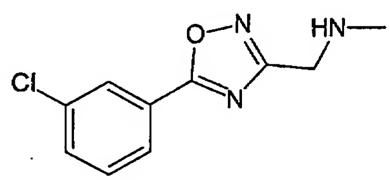


[1000]

[1001] 44.2 g (0.64 mol) of hydroxylamine hydrochloride and 25.5 g (0.64 mol) sodium hydroxide were dissolved in ethanol (500 mL) at r.t. and stirred for 3 h. After filtration, 8.11 g (0.11 mol) 2-hydroxypropanenitrile were added to the filtrate, followed by stirring for 4 h. After concentration to dryness the title compound was obtained which was directly used in the next step. ^{1}H NMR (DMSO-D6): 8.88 (s, 1 H), 5.15 (s, 1 H), 5.02 (s, 1 H), 4.00 (q, 1 H), 1.19 (d, 3 H).

[1002] Example 848

[1003] 1-[5-(3-chlorophenyl)-[1,2,4]oxadiazol-3-yl]-N-methylmethanamine

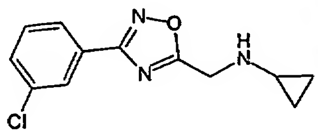
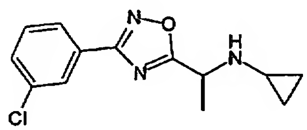
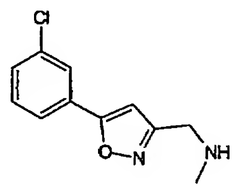
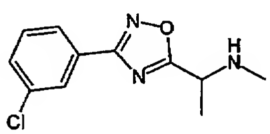
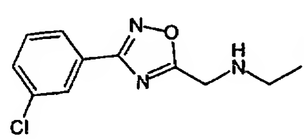


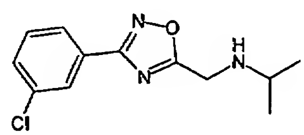
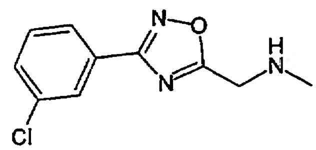
[1004]

[1005] $MeNH_2$ in EtOH (6 mL, 8 M, 48 mmol) was added to 3-(chloromethyl)-5-(3-chlorophenyl)-1,2,4-oxadiazole (1.5 g, 6.5 mmol) in EtOH (20 mL). After 20 h the solvent was evaporated and the residue was dried in vacuum to give 1.47g (100%) of the title compound. LC-MS (M^++1): 224

[1006] The following examples were synthesized in a manner analogous to that for 1-[5-(3-chlorophenyl)-[1,2,4]oxadiazol-3-yl]-N-methylmethanamine.

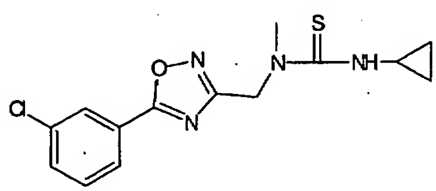
Structure	Name	^{1}H-NMR	Example No.

	[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-ylmethyl]-cyclopropyl-amine	8.05 (s, 1H), 7.95 (d, 1H), 7.42 (d, 1H), 7.39 (t, 1H), 4.08 (s, 2H), 2.89 (m, 1H), 1.75 (brs, 1H), 1.09 (d, 6H).	**849**
	{1-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-ethyl}-cyclopropyl-amine	8.12 (s, 1H), 8 (d, 1H), 7.45 (d, 1H), 7.4 (t, 1H), 4.2 (q, 1H), 2.14 (brs, 1H), 2.04 (m, 1H), 1.54 (d, 3H), 0.43 (brm, 4H).	**850**
	[5-(3-Chloro-phenyl)-isoxazol-3-ylmethyl]-methyl-amine	7.78 (m, 1H), 7.67 (m ,1H), 7.42 (m, 2H), 6.58 (s, 2H), 3.90 (s, 2H), 2.53 (s, 3H).	**851**
	{1-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-ethyl}-methyl-amine	8.03 (s, 1H), 7.9 (d, 1H), 7.41 (d, 1H), 7.37 (t, 1H), 1.04 (q, 1H), 2.4 (s, 3H), 1.6 (br, 1H), 1.51 (d, 3H).	**852**
	[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-ylmethyl]-ethyl-amine	8.02 (s, 1H), 7.9 (d, 1H), 7.42 (d, 1H), 7.35 (t, 1H), 4.06 (s, 2H), 2.72 (q, 2H), 1.73 (br. m, 1H), 1.11 (t, 3H).	**853**

	[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-ylmethyl]-isopropyl-amine	7.98 (s, 1H), 7.87 (d, 1H), 7.35 (d, 1H), 7.31 (t, 1H), 4.04 (s, 2H), 2.23 (brs, 1H), 2.2 (m, 1H), 0.37 (m, 4H).	**854**
	3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-ylmethyl]-methyl-amine	8.13 (S, 1H), 8.00 (d, 1H), 7.52 (dm, 1H), 7.47 (t, 1H), 4.11 (s, 2H), 2.58 (s, 3H).	**855**

[1007] Example 856

[1008] N-{[5-(3-chlorophenyl)-[1,2,4]oxadiazol-3-yl]methyl}-N'-cyclopropyl-N-methylthiourea

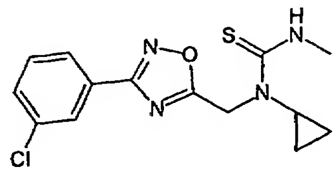
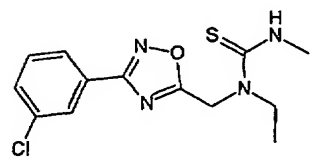
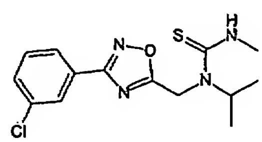
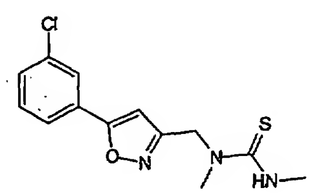


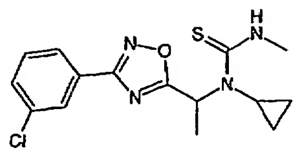
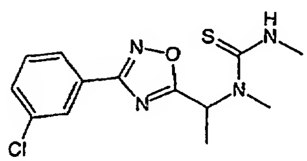
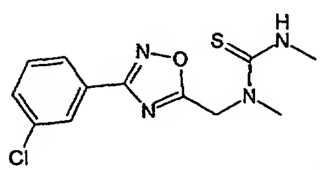
[1009]

[1010] Cyclopropyl isothiocyanate (650 mg, 6.6 mmol) was added to 1-[5-(3-chlorophenyl)-[1,2,4]oxadiazol-3-yl]-N-methylmethanamine (1.47 g, 6.5 mmol) in EtOH (20 mL). After 3 h the formed precipitate was filtrated off and washed with cold EtOH to give 1.63g (78%) of the title compound. LC-MS (M^{+}+1): 323.

[1011] The following examples were synthesized in a manner analogous to that for N-{[5-(3-chlorophenyl)-[1,2,4]oxadiazol-3-yl]methyl}-N'-cyclopropyl-N-methylthiourea.

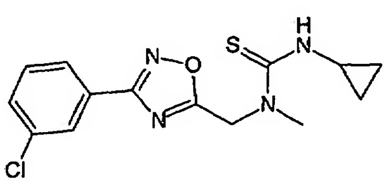
Structure	Name	^{1}H-NMR	Example No.

	1-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-ylmethyl]-1-cyclopropyl-3-methyl-thiourea	8.07 (s, 1H), 7.96 (d, 1H), 7.48 (d, 1H), 7.41 (t, 1H), 6.82 (br, 1H), 5.48 (s, 2H), 3.25 (d, 3H), 2.91 (br, 1H), 1.05 (br, 4H).	857
	1-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-ylmethyl]-1-ethyl-3-methyl-thiourea	8.08 (s, 1H), 7.96 (d, 1H), 7.48 (d, 1H), 7.45 (t, 1H), 6.1 (br, 1H), 5.38 (s, 2H), 3.73 (q, 2H), 3.21 (d, 3H), 1.33 (t, 3H).	858
	1-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-ylmethyl]-1-isopropyl-3-methyl-thiourea	8.05 (s, 1H), 7.93 (d, 1H), 7.48 (d, 1H), 7.42 (t, 1H), 6.45 (br, 1H), 5.04 (s, 2H), 4.96 (m, 1H), 3.21 (d, 3H), 1.26 (m, 4H).	859
	1-[5-(3-Chloro-phenyl)-isoxazol-3-ylmethyl]-1,3-dimethyl-thiourea	^{1}H NMR (DMSO-d6): 7.98 (m, 1H), 7.84 (m ,1H), 7.72 (m, 1H), 7.56 (m, 2H), 7.06 (s, 1H), 5.19 (s, 2H), 3.08 (s, 3H), 2.94 (s, 3H).	860

	1-{1-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-ethyl}-1-cyclopropyl-3-methyl-thiourea	8.00 (s, 1H), 7.98 (d, 1H), 7.47 (d, 1H), 7.44 (t, 1H), 7.25 (m, 1H), 6.84 (br, 1H), 3.26 (d, 3H), 2.55 (br, 1H), 1.9 (d, 3H), 0.91 (br, 2H), 0.76 (br, 2H).	861
	1-{1-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-ethyl}-1,3-dimethyl-thiourea	8.05 (s, 1H), 7.95 (d, 1H), 7.46 (d, 1H), 7.4 (t, 1H), 5.99 (br, 1H), 3.21 (d, 3H), 3.15 (s, 3H), 1.72 (d, 3H), 1.4 (q, 1H).	862
	1-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-ylmethyl]-1,3-dimethyl-thiourea	8.09 (s, 1H), 7.98 (d, 1H), 7.51 (d, 1H), 7.46 (t, 1H), 5.91(w, 1H), 5.55 (s, 2H), 3.32 (s, 3H) and 3.23 (d, 3H).	863

[1012] Example 864

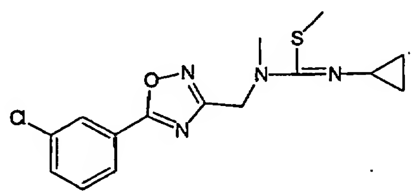
[1013] 1-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-ylmethyl]-3-cyclopropyl-1-methyl-thiourea

[1014] 

[1015] 3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-ylmethyl]-methyl-amine (415 mg, 1.85 mmol) was mixed with cyclopropylisothiocyanate (220 mg, 2.22 mmol) in chloroform (5 mL) at r.t. for 2 hours. The reaction mixture was concentrated and the residue was triturated with Et_2O to yield the title compound (406 mg, 67.9 %). ^{1}H-NMR: 8.09 (s, 1H), 7.98 (d, 1H), 7.51 (d, 1H), 7.46 (t, 1H), 6.00 (w, 1H), 5.53 (s, 2H), 3.28 (s, 3H), 3.11 (m, 1H), 2.45 (s, 3H), 0.94 (m, 2H) and 0.69 (m, 2H).

[1016] Example 865

[1017] Methyl N-{[5-(3-chlorophenyl)-[1,2,4]oxadiazol-3-yl]methyl}-N'-cyclopropyl-N-methylimidothiocarbamate

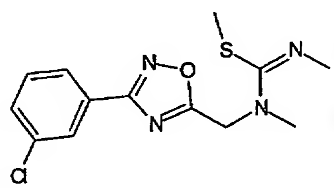
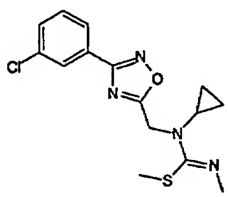
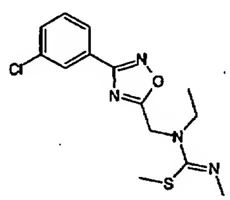
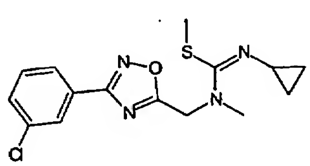


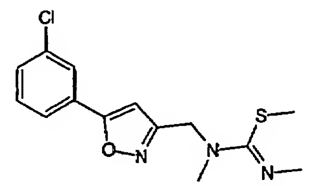
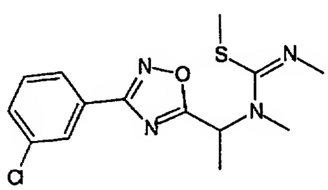
[1018]

[1019] MeI (320 µL, 5.1 mmol) and N-{[5-(3-chlorophenyl)-[1,2,4]oxadiazol-3-yl]methyl}-N'-cyclopropyl-N-methylthiourea (1.59 g, 4.9 mmol) were mixed in EtOH (20 mL) and heated to 70 °C for 2 h. The reaction was cooled to r.t. and NaOH (1M) was added until pH = 10. EA was added and the mixture was stirred for 5 min. The layers were separated and the water phase was extracted with EA. The organic phase was dried and concentrated. The product was purified by column chromatography (Hep-EA 1:1) to afford 960 mg (59%) of the title compound. LC-MS (M^++1): 337

[1020] The following examples were synthesized in a manner analogous to that for methyl N-{[5-(3-chlorophenyl)-[1,2,4]oxadiazol-3-yl]methyl}-N'-cyclopropyl-N-methylimidothiocarbamate.

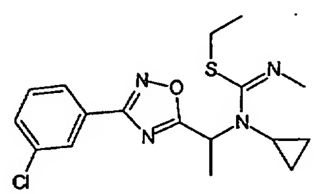
Structure	Name	^{1}H-NMR	Example No.

	1-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-ylmethyl]-1,2,3-trimethyl-isothiourea	8.09 (s, 1H), 7.98 (d, 1H), 7.50 (d, 1H), 7.45 (t, 1H), 4.85 (s, 2H), 3.23 (s, 3H), 3.11 (d, 3H) and 2.37 (s, 3H).	**866**
	1-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-ylmethyl]-1-cyclopropyl-2,3-dimethyl-isothiourea	8.07 (s, 1H), 7.96 (d, 1H), 7.47 (d, 1H), 7.44 (t, 1H), 4.84 (s, 2H), 3.23 (s, 3H), 2.85 (m, 1H), 2.37 (s, 3H), 0.83 (m, 2H), 0.68 (m, 2H).	**867**
	1-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-ylmethyl]-1-ethyl-2,3-dimethyl-isothiourea	8.08 (s, 1H), 7.96 (d, 1H), 7.46 (d, 1H), 7.44 (t, 1H), 4.79 (s, 2H), 3.58 (q, 2H), 3.2 (s, 3H), 2.38 (s, 3H), 1.2 (t, 3H).	**868**
	1-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-ylmethyl]-3-cyclopropyl-1,2-dimethyl-isothiourea	8.09 (s, 1H), 7.98 (d, 1H), 7.51 (d, 1H), 7.44 (t, 1H), 4.78 (s, 2H), 3,17 (m, 1H), 3.13 (s, 3H), 2.43 (s, 3H), 0.72 (m, 2H) and 0.56 (m, 2H).	**869**

	1-[5-(3-Chloro-phenyl)-isoxazol-3-ylmethyl]-1,2,3-trimethyl-isothiourea	7.70 (m, 1H), 7.67 (m ,1H), 7.42 (m, 2H), 6.51 (s, 1H), 4.67 (s,2H), 3.31 (s, 3H), 2.94 (s, 3H), 2.37 (s, 3H).	**870**
	1-{1-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-ethyl}-1,2,3-trimethyl-isothiourea	8.09 (s, 1H), 7.98 (d, 1H), 7.47 (d, 1H), 7.45 (t, 1H), 5.75 (br, 1H), 3.26 (s, 3H), 2.91 (s, 3H), 2.39 (s, 3H), 1.7 (d, 3H).	**871**

[1021] Example 872

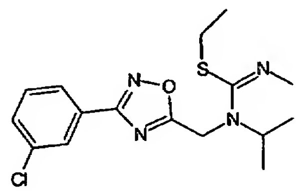
[1022] 1-{1-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-ethyl}-1-cyclopropyl-2-ethyl-3-methyl-isothiourea

[1023] 

[1024] 1-{1-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-ethyl}-1-cyclopropyl-3-methyl-thiourea (287 mg, 0.85 mmol) was mixed with iodoethane (484 mg, 3.4 mmol) in MeOH (5 mL) at 60 °C overnight. The reaction mixture was concentrated and basified with saturated sodium carbonate, then extracted with DCM. The organic layer was dried, concentrated to give the title compound (298 mg, 96 %). ^{1}H-NMR: 8.11 (s, 1H), 8.01 (d, 1H), 7.51 (d, 1H), 7.46 (t, 1H), 5.51 (m, 1H), 3.27 (s, 3H), 2.85-3.00 (m, 2H), 2.60 (m, 1H), 1.79 (d, 3H), 1.30 (t, 3H), 0.83 (m)

[1025] Example 873

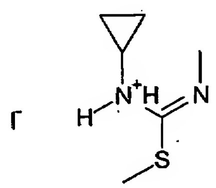
[1026] 1-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-ylmethyl]-2-ethyl-1-isopropyl-3-methyl-isothiourea

[1027] 

[1028] The title compound was synthesized analogous to 1-{1-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-ethyl}-1-cyclopropyl-2-ethyl-3-methyl-isothiourea. ^{1}H-NMR: 8.09 (s, 1H), 7.97 (d, 1H), 7.50 (d, 1H), 7.44 (t, 1H), 4.87 (m, 1H), 4.66 (s, 2H), 3.15 (s, 3H), 2.88 (q, 2H), 1.35 (t, 3H) and 1.23 (s, 6H)

[1029] Example 874

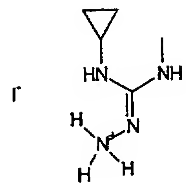
[1030] methyl *N*-cyclopropyl-*N'*-methylimidothiocarbamate hydroiodide

[1031] 

[1032] MeI (265 ml, 4.2 mmol) was added to N-cyclopropyl-N'-methylthiourea (500 mg 3.8 mmol) in acetone (10 ml) and the mixture was heated to reflux. After stirring for 20 min heating was stopped and the solvent was removed under reduced pressure giving the crude title compound in 960 mg yield that was used directly in the next step.

[1033] Example 875

[1034] *N*-cyclopropyl-*N'*-methylcarbonohydrazonic diamide hydroiodide

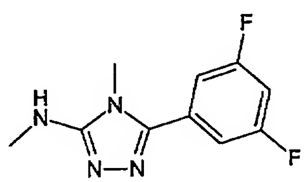


[1035]

[1036] Crude methyl N-cyclopropyl-N'-methylimidothiocarbamate hydroiodide (960 mg, 3.5 mmol) was mixed with hydrazine hydrate (240 ml, 3.9 mmol) in ethanol and heated to reflux for 3 h. The mixure was kept at 7°C for 12 h, yielding crude title compound (0.9 g) which was used directly in the next step.

[1037] Example 876

[1038] 5-(3,5-difluorophenyl)-*N*,4-dimethyl-4*H*-1,2,4-triazol-3-amine

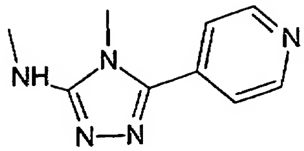


[1039]

[1040] To a solution of methyl N,N'-dimethylimidothiocarbamate hydroiodide (5.0 g, 20.3 mmol) in pyridine (30 ml) was added 3,5-difluorobenzohydrazide (3.5 g, 20.3 mmol) and the mixture was heated to reflux for 24 h. After cooling to r.t. the reaction mixture was poured into ice/H_2O, the formed precipitate was removed via filtration. The filtrate was extracted with $CHCl_3$, the organic phase was dried and concentrated. The residue was washed with Et_2O and then purified by column chromatography using $CHCl_3$:MeOH = 99:1 to 10:1. The title compound was obtained (0.83 g, 18%) together with 3-(3,5-difluorophenyl)-4-methyl-5-(methylthio)-4H-1,2,4-triazole (0.44 g, 9%) as a byproduct. ^{1}H NMR (DMSO-D6): 2.83 (d, 3 H) 3.41 (s, 3 H) 6.20 (d, 1 H) 7.35 (m, 3 H), MS (M^++1) 225.

[1041] Example 877

[1042] Methyl-(4-methyl-5-pyridin-4-yl-4*H*-[1,2,4]triazol-3-yl)-amine

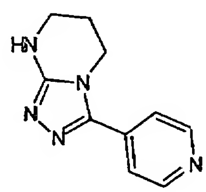


[1043]

[1044] A mixture of 1000 mg (4.35 mmol) N-amino-N',N''-dimethyl-guanidine hydriodide (Henry; Smith; J.Amer.Chem.Soc.; 73; 1951; 1858) and 774 mg (4.35 mmol) isonicotinoyl chloride hydrochloride in pyridine (3 mL) was heated under microwave irradiation for 5 min at 160°C. Aq. sat. K_2CO_3 was added and the mixture was extracted with $CHCl_3$. The organic phase was dried and concentrated. Recrystallization from EtOH, water and EA gave 216 mg (26%) of the title compound. ^{1}H NMR (DMSO-d6): 2.85 (d, 3 H) 3.45 (s, 3 H) 6.25 (d, 1 H) 7.65 (m, 2 H) 8.67 (m, 2 H).

[1045] Example 878

[1046] 3-pyridin-4-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrimidine

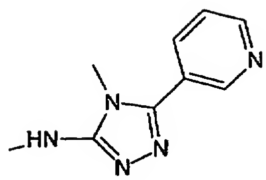


[1047]

[1048] A solution of 750 mg (3.1 mmol) (1,4,5,6-tetrahydro-pyrimidin-2-yl)-hydrazine hydroiodide (Krezel, Izabella; Pharmazie; 1994; p. 27-31) and 552 mg (3.1 mmol) isonicotinoyl chloride hydrochloride in 3 ml pyridine was heated at 120 °C o.n.. The reaction mixture was cooled and diluted with aq. sat. K_2CO_3 and extracted with chloroform. The combined organic extracts were dried and concentrated. Flash chromatography (DCM/MeOH 10:1) afforded 83 mg (18%) of the title compound. ^{1}H NMR: 1.91 (m, 2 H) 3.24 (m, 2 H) 4.13 (m, 2 H) 7.67 (m, 2 H) 8.65 (m, 2 H)

[1049] Example 879

[1050] *N*,4-dimethyl-5-pyridin-3-yl-4*H*-1,2,4-triazol-3-amine

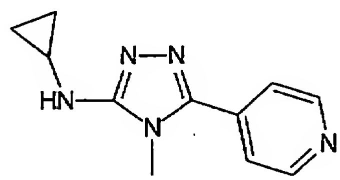


[1051]

[1052] A mixture of N-amino-N',N''-dimethyl-guanidine (500 mg, 2.17 mmol) [J. Amer. Chem. Soc.; 1951; p. 1858] and nicotinoyl chloride hydrochloride (385 mg, 2.17 mmol) in pyridine (10 mL) was refluxed o.n. Aq. sat. K_2CO_3 was added and the mixture extracted with $CHCl_3$. The organic phase was dried and concentrated. The crude product 240 mg (61%) was used in the next step without further purifications. LC-MS (M^++1): 190

[1053] Example 880

[1054] *N*-cyclopropyl-4-methyl-5-pyridin-4-yl-4*H*-1,2,4-triazol-3-amine

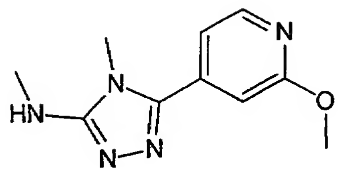


[1055]

[1056] Isonicotinoyl chloride hydrochloride (630 mg, 3.5 mmol) was added to N-cyclopropyl-N'-methylcarbonohydrazonic diamide hydroiodide (900 mg 3.5 mmol) in pyridine (10 ml) and the mixture was stirred at r.t. for 2 h. The mixture was the heated to 160°C under microwave irradiation for 10 min. Water (50 ml) was added and the mixture was extracted with DCM. The pooled organic phases were dried and concentrated and the desired product was obtained by prep. HPLC. LCMS (M^+ +1) 216

[1057] Example 881

[1058] 5-(2-methoxypyridin-4-yl)-*N*,4-dimethyl-4*H*-1,2,4-triazol-3-amine

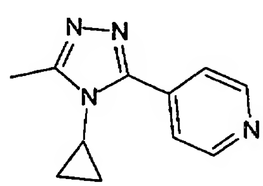


[1059]

[1060] 2-Chloroisonicotinic acid (2.2 g, 13.8 mmol) was refluxed in thionyl chloride (50 ml) for 5 h. The solvent was evaporated (coevaporation with toluene) and the residue was dissolved in pyridine (25 ml) and added in portions to *N,N'*-dimethylcarbonohydrazonic diamide hydroiodide (3.0 g, 13.0 mmol) dissolved in pyridine (25 ml). The reaction mixture was heated at 120°C overnight and the solvent was evaporated, followed by addition of water (10 ml) and filtration. The remaining aq. solution was purified by prep HPLC to give 0.54 g (19%) of the intermediate 5-(2-chloropyridin-4-yl)-*N*,4-dimethyl-4*H*-1,2,4-triazol-3-amine. ^{1}H-NMR (DMSO-d6): 8.51 (dd, 1H), 7.76 (m, 1H), 7.71 (dd, 1H), 6.37 (m, 1H), 3.49 (s, 3H), 2.86 (d, 3 H). This intermediate (0.52g, 2.3 mmol) was dissolved in MeOH (35 ml) and sodium methoxide (4.4 ml of a 30% solution in MeOH, 23.3 mmol) was added. The mixture was refluxed o.n., added to brine and extracted with $CHCl_3$. The combined organic layers were dried ($MgSO_4$) and concentrated to give the title compound (0.28 g, 55 %). ^{1}H NMR (DMSO-d6): 8.26 (d, 1H), 7.27 (dd, 1H), 7.05 (m, 1H), 6.26 (q, 1H), 3.90 (s, 3H), 3.44 (s, 3H), 2.85 (d, 3H).

[1061] Example 882

[1062] 4-(4-cyclopropyl-5-methyl-4*H*-1,2,4-triazol-3-yl)pyridine

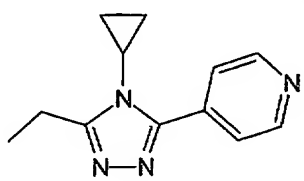
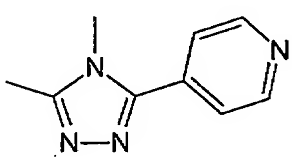


[1063]

[1064] Oxalyl chloride (860 ml, 10 mmol) was slowly added to a solution of N-cyclopropylacetamide (1 g, 10 mmol) [Bouzoubaa, Mohamed, J.Med.Chem.; 28; 7; 1985; 896-900]. and 2,6-lutidine (2.33 ml, 20 mmol) in DCM (30 ml) at r.t. After

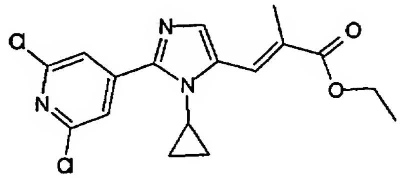
stirring for 30 min isonicotinic acid hydrazide (1.37 g, 10 mmol) was added. The mixture was stirred at r.t. for 3 hours. The solvent was then removed under reduced pressure. Aq. sat. sodium carbonate (15 ml) was added and the mixture was heated to reflux for 2 h, then extracted with EA. The combined organic phases were dried and concentrated. The resulting solid was recrystallized from EA giving the title compound in 1.1 g yield. ^{1}H NMR: 0.7 (m, 2 H) 1.2 (m, 2 H) 2.6 (s, 3 H) 3.3 (ddd, 1 H) 7.7 (m, 2 H) 8.7 (d, 2 H)

[1065] The following examples were synthesized in a manner analogous to that for 4-(4-cyclopropyl-5-methyl-4*H*-1,2,4-triazol-3-yl)pyridine.

Structure	Name	^{1}H-NMR	Example No.
	4-(4-cyclopropyl-5-ethyl-4*H*-1,2,4-triazol-3-yl)pyridine	0.69 (m, 2 H) 1.15 (d, 2 H) 1.48 (t, 3 H) 1.66 (s, 2 H) 2.95 (q, 2 H) 3.28 (s, 1 H) 7.71 (d, 2 H) 8.75 (d, 2 H)	**883**
	4-(4,5-dimethyl-4*H*-1,2,4-triazol-3-yl)pyridine	8.76 (dd, 2 H), 7.52 - 7.63 (m, 2 H), 3.66 (s, 3 H), 2.52 (s, 3 H)	**884**

[1066] Example 885

[1067] 3-[3-Cyclopropyl-2-(2,6-dichloro-pyridin-4-yl)-3H-imidazol-4-yl]-2-methyl-acrylic acid ethyl ester

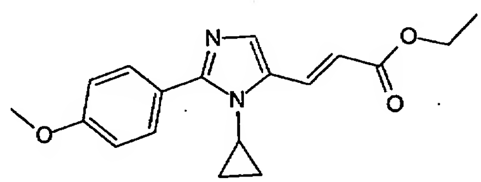


[1068]

[1069] 3-cyclopropyl-2-(2,6-dichloro-pyridin-4-yl)-3H-imidazole-4-carbaldehyde (1.48 g, 5.25 mmol), triethyl-2-phosphonopropionate (1.46 ml, 6.83 mmol) and DBU(1.02 ml, 6.83 mmol) were dissolved in acetonitrile (20 ml). After stirring at 78°C o.n. the reaction mixture was cooled to r.t, diluted with water and extracted with DCM. The combined organic phase was dried (Na_2SO_4), filtered and concentrated *in-vacuo*. The crude was purified on silica gel using 6% EA in DCM, and the isolated residue was triturated with hex. to isolate the title compound (1.66 g, 86%). ^{1}H-NMR: 7.86 (m, 1H), 7.75 (d, 2H), 7.43 (s, 1H), 4.34 (q, 2H), 3.45 (m, 1H), 2.19 (s, 3H), 1.39 (t, 3H), 1.29 (m, 2H), 0.78 (m, 2H).

[1070] Example 886

[1071] 3-[3-Cyclopropyl-2-(4-methoxy-phenyl)-3H-imidazol-4-yl]-acrylic acid ethyl ester

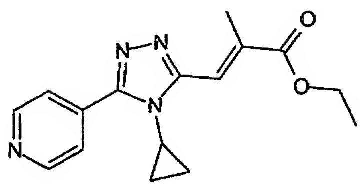


[1072]

[1073] 3-cyclopropyl-2-(4-methoxy-phenyl)-3H-imidazole-4-carbaldehyde (500 mg, 2.06 mmol), triethyl phosphonoacetate (0.53 ml, 2.68 mmol) and DBU (0.40 ml, 2.68 mmol) were dissolved in acetonitrile (5 ml). After stirring at 78°C o.n. the reaction mixture was cooled to r.t., diluted with water (50 ml), extracted with DCM. The combined organic phase was dried (Na_2SO_4), filtered and concentrated *in-vacuo*. Purification of the crude on silica gel using 50% EA in hex. gave the title compound (471 mg, 73%). ^{1}H-NMR: 7.85 (d, 1H), 7.79 (d, 2H), 7.49 (s, 1H), 7.00 (d, 2H), 6.36 (d, 1H), 4.31 (q, 2H), 3.89 (s, 3H), 3.39 (m, 1H), 1.36 (t, 3H), 1.14 (m, 2H), 0.69 (m, 2H).

[1074] Example 887

[1075] 3-(4-Cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-yl)-2-methyl-acrylic acid ethyl ester

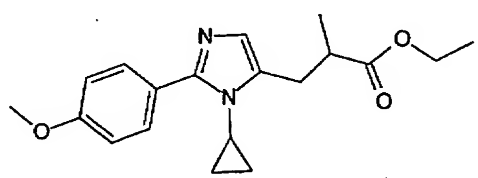


[1076]

[1077] (4-cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-yl)-methanol (6.8 g, 31.4 mmol) was mixed with MnO_2 (40 g, 0.46 mol) in acetonitrile at r.t. for 2 hours and then heated at 80 °C for another 30 min. The reaction mixture was filtered through celite. The filtrate was mixed with 2-(diethoxy-phosphoryl)-propionic acid ethyl ester (12.35 g, 51.8 mmol) and DBU (7.17 g, 47 mmol) at 80 to 90 °C for 4 h. The reaction mixture was concentrated, dissolved in EA and washed with water and brine. The organic layer was dried, concentrated and triturated with hex. to give the title compound in 5.76 g (61 %) yield. ^{1}H-NMR: 8.78(d, 2H), 7.78 (d, 2H), 7.67 (s, 1H), 4.32 (q, 2H), 3.43 (m, 1H), 2.53 (s, 3H), 1.38 (t, 3H), 1.24 (m, 2H) and 0.73 (m, 2H).

[1078] Example 888

[1079] 3-[3-Cyclopropyl-2-(4-methoxy-phenyl)-3H-imidazol-4-yl]-2-methyl-propionic acid ethyl ester



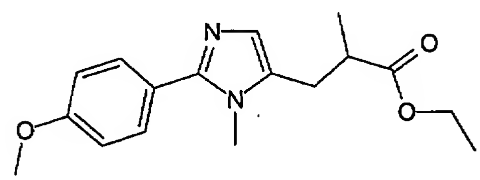
[1080]

[1081] 3-cyclopropyl-2-(4-methoxy-phenyl)-3H-imidazole-4-carbaldehyde (475 mg, 1.96 mmol), triethyl-2-phosphonopropionate (0.63 ml, 2.94 mmol) and DBU (0.44 ml, 2.94 mmol) were dissolved in acetonitrile (5 ml). After stirring at 78 °C o.n. the reaction mixture was cooled to r.t., diluted with water (50 ml) and extracted with DCM. The combined organic phase was dried (Na_2SO_4), filtered and concentrated, to yield 3-[3-cyclopropyl-2-(4-methoxy-phenyl)-3H-imidazol-4-yl]-2-methyl-acrylic acid ethyl ester, which was dissolved in ethanol and hydrogenated at atmospheric pressure over 10% Pd/C (0.5 g) for 24 h. The reaction mixture was filtered through a

celite pad and concentrated. After purification on silica gel (EA/DCM=1/1) the isolated product was dissolved in Et_2O (10 ml) and treated with HCl (1N in Et_2O, 4 ml). The resulting mixture was concentrated and the isolated residue was triturated with Et_2O to isolate the title compound solid (466 mg). ^{1}H-NMR: 7.90 (d, 2H), 7.10 (m, 3H), 4.16 (m, 2H), 3.90 (s, 3H), 3.47 (m, 1H), 3.24 (m, 1H), 2.85 (m, 2H), 1.37 (d, 3H), 1.27 (m, 5H), 0.75 (m, 2H).

[1082] Example 889

[1083] 3-[2-(4-Methoxy-phenyl)-3-methyl-3H-imidazol-4-yl]-2-methyl-propionic acid ethyl ester

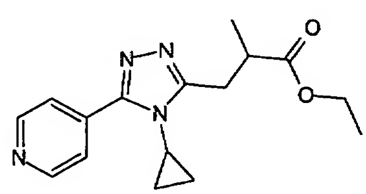


[1084]

[1085] The title compound was synthesized analogous to 3-[3-Cyclopropyl-2-(4-methoxy-phenyl)-3H-imidazol-4-yl]-2-methyl-propionic acid ethyl ester. ^{1}H-NMR: 7.52 (dd, 2H), 6.99 (dd, 2H), 6.88 (s, 1H), 4.15 (q, 2H), 3.87 (s, 3H), 3.59 (s, 3H) 3.00 (m, 1H), 2.80 (m, 1H), 2.67 (m, 1H), 1.27 (m, 6H).

[1086] Example 890

[1087] 3-(4-Cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-yl)-2-methyl-propionic acid ethyl ester

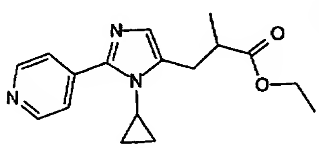
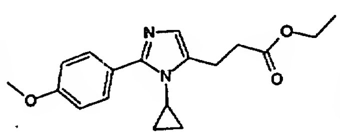


[1088]

[1089] 3-(4-cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-yl)-2-methyl-acrylic acid ethyl ester (5.76 g, 19.3 mmol) was hydrogenated with 10 % Pd / C (3.0 g) in EtOH (100 ml) o.n. The reaction mixture was filtered and concentrated. The residue

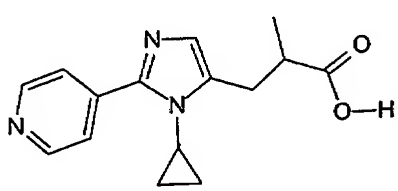
was triturated with hex. to give the title compound in 3.1 g (53 %) yield. ^{1}H-NMR: 8.76 (d, 2H), 7.73 (d, 2H), 4.14(m, 2H), 3.35 (m, 3H), 2.88 (q, 1H), 1.39 (d, 3H), 1.25 (t, 3H), 1.18 (m, 2H) and 0.73 (m, 2H).

[1090] The following examples were synthesized analogous to 3-(4-Cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-yl)-2-methyl-propionic acid ethyl ester

Structure	Name	^{1}H-NMR	Example No.
	3-(3-Cyclopropyl-2-pyridin-4-yl-3H-imidazol-4-yl)-2-methyl-propionic acid ethyl ester	8.69 (dd, 2H), 7.68 (dd, 2H), 6.91 (s, 1H), 4.16 (q, 2H), 3.33 (m, 1H), 3.19 (m, 1H), 2.85 (m, 2H), 1.33 (d, 3H), 1.25 (t, 3H), 1.14 (m, 2H), 0.69 (m, 2H).	891
	3-[3-Cyclopropyl-2-(4-methoxy-phenyl)-3H-imidazol-4-yl]-propionic acidethyl ester	7.66 (d, 2H), 6.95 (d, 2H), 6.80 (br. s, 1H), 4.20 (q, 2H), 3.88 (s, 3H), 3.23 (m, 1H), 3.05 (m, 2H), 2.76 (m, 2H), 1.30 (t, 3H), 1.03 (m, 2H), 0.65 (m, 2H).	892

[1091] Example 893

[1092] 3-(3-Cyclopropyl-2-pyridin-4-yl-3H-imidazol-4-yl)-2-methyl-propionic acid



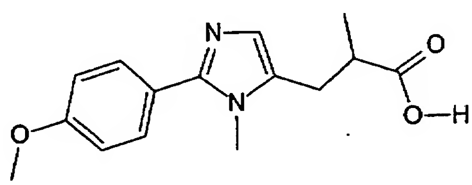
[1093]

[1094] 3-(3-cyclopropyl-2-pyridin-4-yl-3H-imidazol-4-yl)-2-methyl-propionic acid

ethyl ester (1.02 g, 3.40 mmol) was mixed with MeOH (8 ml) and sodium hydroxide (1N in water, 5.1 ml, 5.10 mmol). This mixture was left stirring at r.t. for 5 h, followed by concentration *in-vacuo*. The isolated residue was treated with aq. HCl (2N, 6 ml) to isolate the title compound (702 mg, 76%). ^{1}H-NMR (DMSO-d6): 8.63 (dd, 2H), 7.74 (dd, 2H), 6.82 (s, 1H), 3.55 (m, 1H), 3.09 (m, 1H), 2.82 (m, 2H), 1.19 (d, 3H), 1.08 (m, 2H), 0.56 (m, 2H).

[1095] Example 894

[1096] 3-[2-(4-Methoxy-phenyl)-3-methyl-3H-midazol-4-yl]-2-methyl-propionic acid

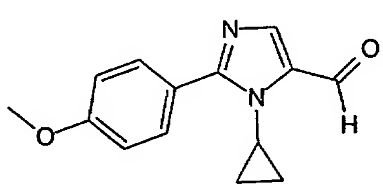


[1097]

[1098] The title compound was synthesized analogous to 3-(3-Cyclopropyl-2-pyridin-4-yl-3H-imidazol-4-yl)-2-methyl-propionic acid. ^{1}H-NMR (DMSO-d6):7.52 (d, 2H), 7.02 (d, 2H), 6.71 (s, 1H), 3.80 (s, 3H), 3.55 (s, 3H) 2.89 (m, 1H), 2.67 (m, 2H), 1.15 (d, 3H).

[1099] Example 895

[1100] 3-Cyclopropyl-2-(4-methoxy-phenyl)-3H-imidazole-4-carbaldehyde

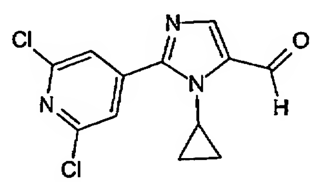
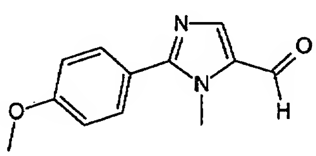


[1101]

[1102] N-cyclopropyl-4-methoxy-benzamidine (0.90 g, 4.75 mmol), 2-bromo-3-isopropoxy-propenal (1.37 g, 7.12 mmol) and K_2CO_3 (0.98 g, 7.12 mmol) were mixed with chloroform (10 ml) and water (1.2 ml), followed by stirring at r.t. for 24 h. After drying of the reaction mixture (Na_2SO_4), filtration and concentration of the filterate

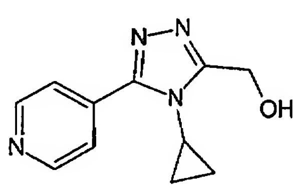
in-vacuo, the crude residue was purified via flash chromatography (40% EA in hex.) to isolate the title compound (973 mg, 85%). ^{1}H-NMR: 9.83 (s, 1H), 7.82 (m, 3H), 7.02 (d, 2H), 3.89 (s, 3H), 3.58 (m, 1H), 1.13 (m, 2H), 0.64 (m, 2H).

[1103] The following examples were synthesized in a manner analogous to that for 3-Cyclopropyl-2-(4-methoxy-phenyl)-3H-imidazole-4-carbaldehyde.

Structure	Name	^{1}H-NMR	Example No.
	3-Cyclopropyl-2-(2,6-dichloro-pyridin-4-yl)-3H-imidazole-4-carbaldehyde	9.92 (s, 1H), 7.88 (s, 1H), 7.79 (s, 2H), 3.65 (m, 1H), 1.33 (m, 2H), 0.72 (m, 2H).	896
	2-(4-methoxy-phenyl)-3-methyl-3H-imidazole-4-carbaldehyde	9.77 (s, 1H), 7.87 (s, 1H), 7.63 (dd, 2H), 7.04 (dd, 2H), 4.02 (s, 3H), 3.89 (s, 3H).	897

[1104] Example 898

[1105] (4-Cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-yl)-methanol



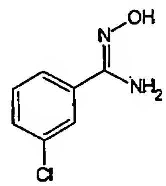
[1106]

[1107] 4-(4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine (6.85 g, 36.8 mmol) was mixed with 37 % formaldehyde (30 mL) in a sealed vial and heated at 135 °C o.n. The reaction mixture was concentrated with silica gel and then mixed with MeOH. The mixture was filtered and washed with MeOH. The filtrate was concentrated with

silica gel again and loaded on a flash column and eluted with 10 % MeOH (2 M NH_3) in DCM to give the title compound (6.8 g, 85 %). ^{1}H-NMR(DMSO-d_6): 8.75(d, 2H), 7.84 (d, 2H), 5.63 (t, 1H), 4.72 (d, 2H), 3.66 (m, 1H), 1.04 (m, 2H), 0.73 (m, 2H).

[1108] Example 899

[1109] 3-chloro-N'-hydroxybenzenecarboximidamide

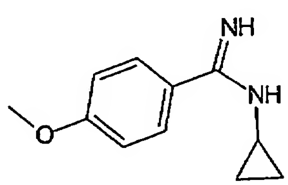


[1110]

[1111] A solution of 3.35 mL (30.0 mmol) 3-chlorobenzonitrile in ethanol (40 mL) was added to a solution of 2.47 g (35.5 mmol) hydroxylamine hydrochloride and 1.42 g (35.5 mmol) NaOH in water (20 mL) at r.t. and then heated at 90°C for 24 h. After cooling, the reaction mixture was concentrated, the residue diluted with water, followed by filtration and drying to afford 1.13 g (93%) of the title compound. ^{1}H NMR: 8.11 (s, 1H), 7.72 (s, 1H), 7.61 (m, 1H), 7.46 (m, 1H), 7.36 (m, 1H).

[1112] Example 900

[1113] N-Cyclopropyl-4-methoxy-benzamidine



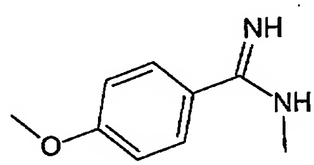
[1114]

[1115] 4-methoxy-benzimidic acid ethyl ester hydrochloride (1.25 g, 5.8 mmol), DCM (5 ml) and cyclopropylamine (0.92 ml, 13.3 mmol) were mixed. After stirring at r.t for 3 h, the reaction mixture was concentrated *in-vacuo*. The residue was treated with cold aq. sodium hydroxide (1M) and extracted with EA. The combined organic phase was washed with water and brine, dried (Na_2SO_4), filtered and concentrated *in-vacuo*, to isolate the title compound (0.90 g, 82%). ^{1}H-NMR: 7.64

(d, 2H), 6.90 (d, 2H), 5.3 (bs, 2H), 3.85 (s, 3H), 2.59 (m, 1H), 0.84 (m, 2H), 0.62 (m, 2H).

[1116] Example 901

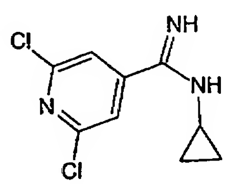
[1117] 4-Methoxy-N-methyl-benzamidine

[1118] 

[1119] Methylamine hydrochloride (2.28 g, 33.8 mmol) was suspended in toluene (16 ml). After cooling the resulting mixture to 0°C, trimethylaluminum (2M in toluene) was added drop-wise under Ar, followed by warming the mixture to r.t and stirring for 2 h. To this mixture was then added a solution of 4-methoxybenzonitrile in toluene (16 ml), followed by stirring at 80°C for 24 h. The reaction mixture was cooled to r.t. and slowly poured in to a slurry of silica gel (10 g) in $CHCl_3$ (75 ml). The slurry was stirred at r.t for 15 minutes and filtered using MeOH. The filtrate was concentrated. The isolated residue was dissolved in water (50 ml) and extracted with $CHCl_3$. The combined organic phase was washed with brine, dried (Na_2SO_4), filtered and concentrated *in-vacuo*, to isolate the title compound (1.25 g). ^{1}H-NMR (DMSO-d6): 7.68 (d, 2H), 6.91 (dd, 2H), 6.33 (br. s, 2H), 3.77 (s, 3H), 2.77 (s, 3H)

[1120] Example 902

[1121] 2,6-Dichloro-N-cyclopropyl-isonicotinamidine

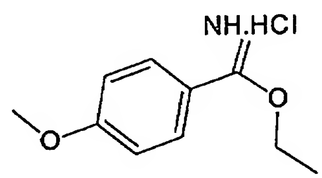
[1122] 

[1123] 2,6-dichloropyridine-4-carbonitrile (5 g, 28.9 mmol), methanol (50 ml) and sodium methoxide (0.66 ml, 2.89 mmol) were mixed and stirred at r.t. for 3 h. HCl in

EtOH (24% w/w, 10 ml) and cyclopropylamine (3 mL, 43.4 mmol) were added at 0°C, followed by stirring at r.t. o.n. The reaction mixture was concentrated *in-vacuo*. The isolated residue was treated with cold aq. NaOH (1N, 75 ml) and extracted with EA. The combined organic phase was washed sequentially with aq. NaOH and brine, dried (Na_2SO_4), filtered and concentrated *in-vacuo*. The isolated residue was triturated with Et_2O to isolate the title compound (3.82 g). ^{1}H-NMR: 7.59 (br. s, 2H), 4.96 (br. s, 2H), 2.60 (m, 1H), 0.90 (m, 2H), 0.69 (m, 2H).

[1124] Example 903

[1125] 4-Methoxy-benzimidic acid ethyl ester hydrochloride

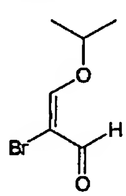


[1126]

[1127] 4-Methoxybenzonitrile and 24% hydrochloric acid in EtOH were mixed at 0°C. This mixture was left stirring at r.t. o.n., followed by concentration *in-vacuo*. The isolated residue was triturated with Et_2O to isolate the title compound (1.25 g). ^{1}H-NMR: 12.3 (br. s, 1H), 11.6 (br. s, 1H), 8.43 (d, 2H), 7.04 (d, 2H), 4.91 (t, 3H), 3.90 (s, 3H), 1.61 (t, 3H).

[1128] Example 904

[1129] 2-Bromo-3-isopropoxy-propenal



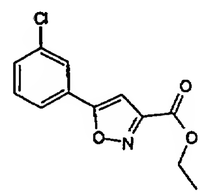
[1130]

[1131] A mixture of 2-bromomalonaldehyde, *para*-toluenesulfonic acid monohydrate, 2-propanol and cyclohexane were stirred at 86°C in flask with a dean-stark trap under azeotropic conditions. Further distillation removed another 40% of

the original solvent volume. The mixture was cooled to 0°C, then concentrated *in-vacuo*, to isolate the title compound (13.2 g). ^{1}H-NMR: 9.16 (s, 1H), 7.65 (s, 1H), 4.51 (m, 1H), 1.47 (d, 6H).

[1132] Example 905

[1133] 5-(3-chloro-phenyl)-isoxazole-3-carboxylic acid ethyl ester

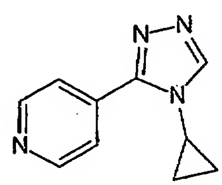


[1134]

[1135] A solution of 4-(3-chloro-phenyl)-2,4-dioxo-butyric acid ethyl ester (3.0 g, 11.8 mmol) and hydroxylamine hydrochloride (2.46 g, 35.4 mmol) in MeOH (60 mL) was heated at 80°C for 4 h. After cooling, the mixture was filtered and washed with cold MeOH to afford the title compound (2.0 g, 71%). ^{1}H NMR: 7.82 (s, 1H), 7.72 (m, 1H), 7.47 (m, 2H), 4.03 (s, 3H).

[1136] Example 906

[1137] 4-(4-Cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine

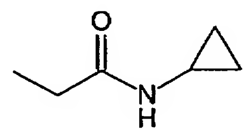


[1138]

[1139] 4-cyclopropyl-5-pyridin-4-yl-2,4-dihydro-3H-1,2,4-triazole-3-thione (11.11 g, 51 mmol) was slowly added to wet Raney nickel (90 g) in EtOH (200 mL) in portions. The reaction mixture was heated at 60 °C for 3.5 h and then filtered through celite. The filtrate was concentrated to give the title compound (6.85 g, 72.3 %). ^{1}H-NMR: 8.76 (d, 2H), 8.71 (s, 1H), 7.95 (d, 2H), 3.75(m, 1H), 1.08 (m, 2H) and 0.94 (m, 2H).

[1140] Example 907

[1141] *N*-cyclopropylpropanamide

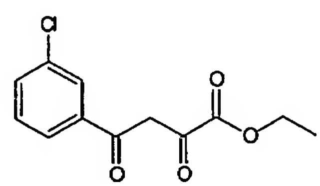


[1142]

[1143] A solution of propionic anhydride (6.41 ml, 50.0 mmol) and cyclopropylamine (3.48 ml, 50.0 mmol) in benzene (50 ml) was heated to reflux for 6 h and then the solvent was evaporated. Recrystallization from EA/hex. afforded the title compound (1.45 g, 26%). ^{1}H NMR: 0.48 (m, 2 H) 0.76 (m, 2 H) 1.13 (t, 3 H) 2.14 (q, 2 H) 2.69 (m, 1 H)

[1144] Example 908

[1145] 4-(3-Chloro-phenyl)-2,4-dioxo-butyric acid ethyl ester

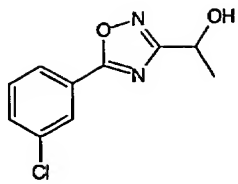


[1146]

[1147] Sodium hydride (60% oil dispersion, 1.24 g, 31.1 mmol) was added in portions to a solution of 3-chloroacetophenone (4.0 g, 25.9 mmol) and diethyl oxalate (4.54 g, 31.1 mmol) in DMF (32 mL) at 0°C. The mixture was stirred at r.t for 1 h and was then heated at 80°C for 0.5 h. After cooling, the mixture was treated with 3N HCl and then diluted with EA. The organic layer was washed with water and saturated brine, dried (Na_2SO_4), filtered and concentrated. The resulting residue was then purified by column chromatography using 0 – 10% EA in hex to afford the title compound (4.43g, 67%). ^{1}H NMR: 15.12 (br s, 1H), 7.98 (s, 1H), 7.88 (d, 1H), 7.58 (d, 1H), 7.47 (t, 1H), 7.05 (s, 1H), 4.39 (m, 2H), 1.41 (m, 3H).

[1148] Example 909

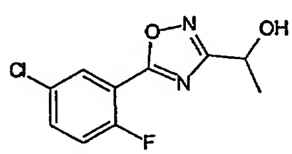
[1149] 1-[5-(3-chlorophenyl)-[1,2,4]oxadiazol-3-yl]ethanol

[1150] 

[1151] 27.2 g crude N'-[(3-chlorobenzoyl)oxy]-2-hydroxypropanimidamide was dissolved in ethanol (250 mL) and refluxed for 1 h, followed by addition of 14.0 g (170 mmol) sodium acetate in water (40 mL). After refluxing o.n., cooling to r.t. and addition of water (250 mL) the mixture was concentrated *in vacuo* to about ½ of its volume, resulting in a precipitate which was filtered off and recrystallized from EA/Hep to yield 6.45 g (25%) of the title compound. ^{1}H NMR: 8.14 (s, 1 H), 8.02 (d, 1 H), 7.57 (d, 1 H), 7.47 (t, 1 H), 5.04 - 5.14 (m, 1 H), 2.51 (d, 1 H), 1.67 (d, 3 H)

[1152] Example 910

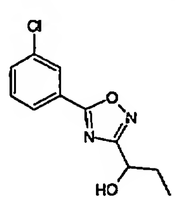
[1153] 1-[5-(5-chloro-2-fluorophenyl)-1,2,4-oxadiazol-3-yl]ethanol

[1154] 

[1155] The title compound was synthesized analogous to 1-[5-(3-chlorophenyl)-[1,2,4]oxadiazol-3-yl]ethanol. ^{1}H-NMR: 8.12 (dd, 1 H), 7.49 - 7.58 (m, 1 H), 7.18 - 7.27 (m, 1 H), 5.12 (q, 1 H), 1.68 (d, 3 H)

[1156] Example 911

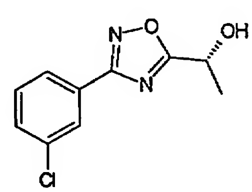
[1157] 1-[5-(3-chlorophenyl)-[1,2,4]oxadiazol-3-yl]propan-1-ol

[1158] 

[1159] Propionaldehyde cyanohydrin (9.62 g, 113 mmol) was added slowly to hydroxyl amine (100 ml, 1.27 M in EtOH) at 0 °C. Stirring was continued at r.t. for 3 h and then the reaction mixture was concentrated to dryness under reduced pressure to give crude (E/Z)-N',2-dihydroxybutanimidamide (9.1 g, 68%). Crude (E/Z)-N',2-dihydroxybutanimidamide (8.0 g, 67.7 mmol) was dissolved in pyridine (350 ml) and 3-chlorobenzoyl chloride (8.72 ml, 67.7 mmol) was added slowly at 0 °C. After stirring at r.t. for 1 h the mixture was heated at reflux o.n. After cooling to r.t. sat. aq. $NaHCO_3$ was added and the mixture was extracted with DCM. The organic phase was washed with water and brine, dried and concentrated. Column chromatography (hep/EA 4:1) gave 7.15 g (44 %) of the title compound. ^{1}H NMR: 1.04 (t, 3 H) 2.00 (m, 2 H) 2.35 (m, 1 H) 4.87 (m, 1 H) 7.47 (t, 1 H) 7.57 (m, 1 H) 8.02 (m, 1 H) 8.14 (m, 1 H)

[1160] Example 912

[1161] (+)-(1R)-1-[3-(3-chlorophenyl)-1,2,4-oxadiazol-5-yl]ethanol

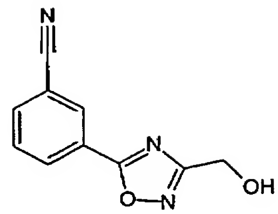


[1162]

[1163] A solution of 1.53 g (18.6 mmol) sodium acetate in water (12 mL) was added to 3.88 g (16.0 mmol) 3-chloro-N'-{[(2R)-2-hydroxypropanoyl]oxy}benzenecarboximidamide dissolved in ethanol (50 mL). The mixture was heated to 90°C for 5.5 h and then evaporated to dryness and purified via flash chromatography (Hep/EA = 9/1) to give after drying 2.3 g (65%) of the title compound. ^{1}H NMR: 8.09 (t, 1 H), 7.97 (td, 1 H), 7.45 - 7.51 (m, 1 H), 7.42 (t, 1 H), 5.15 (qd, 1 H), 2.57 (d, 1 H), 1.72 (d, 3 H)

[1164] Example 913

[1165] 3-[3-(hydroxymethyl)-1,2,4-oxadiazol-5-yl]benzonitrile

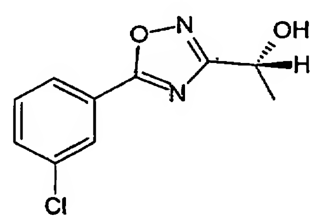


[1166]

[1167] Hydroxylamine (50% aq., 5.7 g, 172 mmol) was added drop-wise to a solution of hydroxyacetonitrile (55% aq., 8.9 g, 156 mmol) in water (100 ml) and stirred at rt for 4 h. Water was evaporated and the residue was dissolved in EtOH and dried (Na_2SO_4). 3-Cyanobenzoyl chloride (9.5 g, 57.1 mmol) in THF (10 ml) was added drop-wise to a slurry of the obtained crude (1E)-N',2-dihydroxyethanimidamide (4.7 g, 51.9 mmol) and DEA (8.0 g, 62.3 mmol) in THF (10 ml) at 0°C. The reaction mixture was stirred at 0°C for 2 h, diluted with Et_2O (100 ml) and washed (NH_4Cl aq.). The water phase was extracted with Et_2O and the organic layers were dried (Na2sO4). The obtained crude (1E)-N'-[(3-cyanobenzoyl)oxy]-2-hydroxyethanimidamide (5.0 g, 22.8 mmol) was dissolved in EtOH (50 ml). NaOAc (2.8 g, 34.2 mmol) was added and the mixture was refluxed o.n. The reaction mixture was concentrated and the precipitate recrystallized from EtOH (10 ml) to give the title compound (1.4 g). ^{1}H NMR (DMSO-d6): 8.51 (m, 1 H), 8.39 (m, 1 H), 8.16 (m, 1 H), 7.84 (t, 1 H), 5.78 (t, 1 H), 4.63 (t, 2 H).

[1168] Example 914

[1169] (+)-(1R)-1-[5-(3-chlorophenyl)-[1,2,4]oxadiazol-3-yl]ethanol



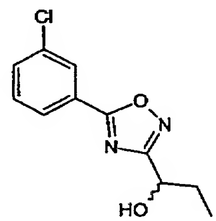
[1170]

[1171] 7.13 g (26.7 mmol) (+)-(1R)-1-[5-(3-chlorophenyl)-[1,2,4]oxadiazol-3-yl]ethyl acetate and 2.33 g (56.7 mmol) lithium hydroxide monohydrate were mixed with 1:1 THF/Water (100mL) and stirred for 18 h. Reducing the volume of the

mixture *in vacuo* to about ½, followed by dilution with brine and extraction with ethyl acetate. 5.8 g (97%) of the title compound was obtained after evaporation and drying. ^{1}H NMR: 8.14 (s, 1 H), 8.02 (d, 1 H), 7.57 (d, 1 H), 7.47 (t, 1 H), 5.04 - 5.14 (m, 1 H), 2.42 (br s, 1 H), 1.67 (d, 3 H)

[1172] Example 915

[1173] (+)-1-[5-(3-chlorophenyl)-[1,2,4]oxadiazol-3-yl]propan-1-ol

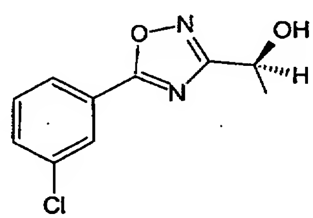


[1174]

[1175] The title compound was synthesized analogous to (+)-(1R)-1-[5-(3-chlorophenyl)-[1,2,4]oxadiazol-3-yl]ethanol and was used directly in the next step for (+)-4-(5-{1-[5-(3-chlorophenyl)-1,2,4-oxadiazol-3-yl]propoxy}-4-methyl-4H-1,2,4-triazol-3-yl)pyridine.

[1176] Example 916

[1177] (-)-(1S)-1-[5-(3-chlorophenyl)-[1,2,4]oxadiazol-3-yl]ethanol

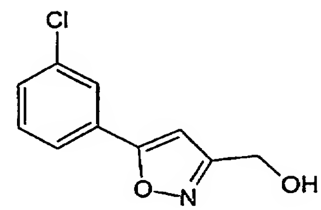


[1178]

[1179] The title compound was isolated from the reaction as described for the synthesis of (+)-(1R)-1-[5-(3-chlorophenyl)-[1,2,4]oxadiazol-3-yl]ethyl acetate. Isolation took place during DCM elution of the column chromatography, yielding 5 g (50%) of the title compound. ^{1}H NMR: 8.14 (s, 1 H), 8.02 (d, 1 H), 7.57 (d, 1 H), 7.47 (t, 1 H), 5.04 - 5.14 (m, 1 H), 2.51 (d, 1 H), 1.67 (d, 3 H).

[1180] Example 917

[1181] [5-(3-Chloro-phenyl)-isoxazol-3-yl]-methanol

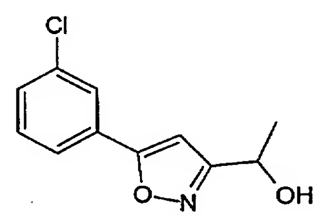


[1182]

[1183] Lithium aluminum hydride (320 mg, 8.4 mmol) was slowly added to a solution of 5-(3-chloro-phenyl)-isoxazole-3-carboxylic acid ethyl ester (2.0 g, 8.4) in THF (100 ml) at r.t After 1 h, the reaction mixture was quenched with water and then extracted with EA. The organic layer was washed with water and brine, dried (Na_2SO_4), filtered, and concentrated. The resulting residue was then purified by column chromatography using 15-40% EA in hex. to afford the title compound (1.32g, 75%,). ^{1}H NMR: 7.78 (s, 1H), 7.68 (m, 1H), 7.43 (m, 2H), 6.63 (s, 1H), 4.84 (d, 2H), 2.23 (t, 1H).

[1184] Example 918

[1185] 1-[5-(3-Chloro-phenyl)-isoxazol-3-yl]-ethanol



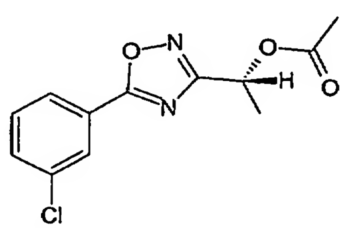
[1186]

[1187] Step 1: 5-(3-Chloro-phenyl)-isoxazole-3-carboxylic acid methyl ester: A solution of 4-(3-chloro-phenyl)-2,4-dioxo-butyric acid ethyl ester (3.0 g, 11.8 mmol) and hydroxylamine hydrochloride (2.46 g, 35.4 mmol) in MeOH (60 ml) was heated at 80°C for 4 h. After cooling, the mixture was filtered and washed with cold methanol to afford 5-(3-chloro-phenyl)-isoxazole-3-carboxylic acid methyl ester (2.0 g, 71%). ^{1}H NMR: 7.82 (s, 1H), 7.72 (m, 1H), 7.47 (m, 2H), 4.03 (s, 3H). Step 2: 1-[5-(3-Chloro-phenyl)-isoxazol-3-yl]-ethanone: In a screw cap vial equipped with

stir bar was mixed methyl magnesium iodide (3M in Et_2O) (0.79 ml, 2.38 mmol), toluene (1 ml), tetrahydrofuran (0.39 ml, 4.77 mmol) and TEA (1 ml, 7.15 mmol). After cooling to 0°C a solution of 5-(3-chloro-phenyl)-isoxazole-3-carboxylic acid methyl ester (300 mg, 1.19 mmol) in toluene (5 ml) was added, followed by stirring at 0°C for 5 h. The mixture was then quenched with aq 1N HCl (6.5 ml, 6.5 mmol), diluted with toluene (35 ml), sequentially washed with water, sat. aq. sodium bicarbonate, water and brine. The organic phase was concentrated *in-vacuo*. The isolated residue was dissolved in MeOH (8 ml) and 20% aq. KOH (1 ml) was added, followed by stirring at 45°C for 30 min and then concentrated *in-vacuo*. The residue was dissolved in toluene (60 ml), sequentially washed with water, sat. aq. sodium bicarbonate and water. The organic phase was concentrated *in-vacuo*. The crude residue was purified on silica gel using 2% EA in hex. to isolate the desired compound (156 mg, 60%). ^{1}H-NMR: 7.77 (m, 1H), 7.66 (m, 1H), 7.42 (m, 2H), 6.90 (s, 1H), 2.69 (s, 3H). Step 3: 1-[5-(3-Chloro-phenyl)-isoxazol-3-yl]-ethanol: In a screw cap vial equipped with stir bar was mixed 1-[5-(3-chloro-phenyl)-isoxazol-3-yl]-ethanone (100 mg, 0.45 mmol), sodium borohydride (34 mg, 0.90 mmol) and MeOH (3 ml), followed by stirring at r.t for 3 h and the quenched with water and brine, extracted with DCM. The combined organic phase was dried (Na_2SO_4), filtered and concentrated *in-vacuo* to isolate the title compound .^{1}H-NMR: 7.69 (m, 1H), 7.59 (m, 1H), 7.37 (m, 2H), 6.59 (s, 1H), 5.07 (q, 1H), 3.45 (br. s, 1H), 1.58 (d, 3H).

[1188] Example 919

[1189] (+)-(1R)-1-[5-(3-chlorophenyl)-[1,2,4]oxadiazol-3-yl]ethyl acetate



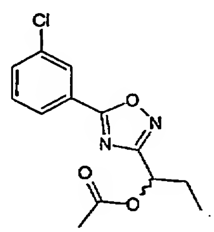
[1190]

[1191] 12.1 g (53.9 mmol) 1-[5-(3-chlorophenyl)-[1,2,4]oxadiazol-3-yl]ethanol and 1.60 g Novozyme 435® are taken up under Ar in toluene (750 mL). After addition of

5.0 mL (54.2 mmol) vinyl acetate the reaction was run at r.t. o.n., followed by filtration over celite and washing with DCM. The filtrate was purified over silica using DCM neat, followed by EA/Hep = 1/1, yielding 7.1 g (49%) of the title compound. ^{1}H NMR: 8.13 (t, 1 H), 8.01 (d, 1 H), 7.55 (d, 1 H), 7.47 (t, 1 H), 6.07 (q, 1 H), 2.15 (s, 3 H), 1.69 (d, 3 H)

[1192] Example 920

[1193] (+)-1-[5-(3-chlorophenyl)-[1,2,4]oxadiazol-3-yl]propyl acetate

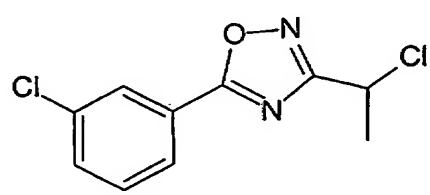


[1194]

[1195] The title compound was prepared analogous to (+)-(1R)-1-[5-(3-chlorophenyl)-[1,2,4]oxadiazol-3-yl]ethyl acetate with stirring at 70 °C for 6 h. ^{1}H NMR: 1.00 (t, 3 H) 2.07 (m, 2 H) 2.16 (s, 3 H) 5.90 (t, 1 H) 7.46 (t, 1 H) 7.52 - 7.59 (m, 1 H) 7.98 - 8.06 (m, 1 H) 8.13 (t, 1 H)

[1196] Example 921

[1197] 3-(1-chloroethyl)-5-(3-chlorophenyl)-[1,2,4]oxadiazole

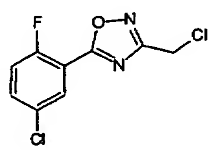
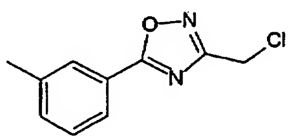


[1198]

[1199] 5 drops of DMF were added to 1-[5-(3-chlorophenyl)-[1,2,4]oxadiazol-3-yl]ethanol (12.3 g, 54.9 mmol) in $SOCl_2$ (150 mL) and the reaction was heated at 70 °C for 5 h. The excess $SOCl_2$ was evaporated and the residue was purified by column chromatography (Hep 100% to Hep/EA=5/1) to give 12.4 g (93 %) of the title

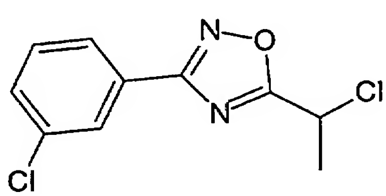
compound. ^{1}H NMR: 1.96 (d, 3H) 5.20 (q, 1H) 7.46 (t, 1H) 7.59 (m, 1H) 8.04 (m, 1H) 8.17 (t, 1H)

[1200] The following examples were synthesized in a manner analogous to that for 3-(1-chloroethyl)-5-(3-chlorophenyl)-[1,2,4]oxadiazole.

Structure	Name	^{1}H-NMR	Example No.
	5-(5-Chloro-2-fluoro-phenyl)-3-chloromethyl-[1,2,4]oxadiazole	8.16 (m, 1H), 7.58 (m, 1H), 7.29 (m, 1H), 4.72 (s, 3H).	922
	3-Chloromethyl-5-(3-methyl-phenyl)-[1,2,4]oxadiazole	7.93 (m, 2H), 7.40 (m, 2H), 4.67 (s, 2H), 2.39 (s, 3H).	923

[1201] Example 924

[1202] 5-(1-chloroethyl)-3-(3-chlorophenyl)-[1,2,4]oxadiazole



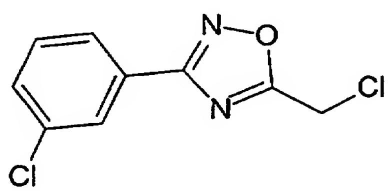
[1203]

[1204] 1.80 g 3-chloro-N'-hydroxybenzenecarboximidamide and 3.7 mL DEA were dissolved under Ar in DCM (100 mL) and cooled on an ice/water bath, followed by

addition of 2-chloropropanoyl chloride. After 1h at r.t. the mixture was concentrated and the crude taken up in DMF (120 mL), followed by heating for at 120 °C for 2h. The mixture was concentrated onto celite and purified via column chromatography (hep 100% to hep/EA = 7/3) yielding the title compound (1.72 g, 67%). ^{1}H NMR: 8.09 (t, 1 H), 7.93 - 8.02 (m, 1 H), 7.38 - 7.54 (m, 2 H), 5.22 (q, 1 H), 2.02 (d, 3 H)

[1205] Example 925

[1206] 5-Chloromethyl-3-(3-chloro-phenyl)-[1,2,4]oxadiazole

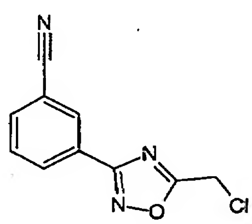


[1207]

[1208] The title compound was prepared analogous to 5-(1-chloroethyl)-3-(3-chlorophenyl)-[1,2,4]oxadiazole. ^{1}H NMR: 8.07 (t, 1 H), 7.93 - 7.98 (m, 1 H), 7.46 - 7.52 (m, 1 H), 7.42 (t, 1 H), 4.74 (s, 2 H)

[1209] Example 926

[1210] 3-[5-(chloromethyl)-1,2,4-oxadiazol-3-yl]benzonitrile

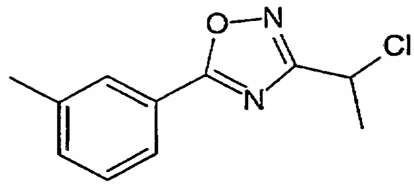


[1211]

[1212] The title compound was prepared analogous to 5-(1-chloroethyl)-3-(3-chlorophenyl)-[1,2,4]oxadiazole. ^{1}H NMR: 8.40 (s, 1H), 8.32 (d, 1H), 7.82 (d, 1H), 7.64 (t, 1H), 4.77 (s, 2H).

[1213] Example 927

[1214] 3-(1-chloro-ethyl)-5-m-tolyl-[1,2,4]oxadiazole

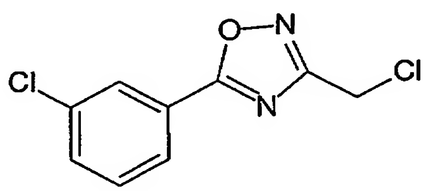


[1215]

[1216] 2-Chloro-N-hydroxy-propionamidine (218 mg, 1.78 mmol) and triethylamine (0.677 ml, 4.86 mmol) were added to 3-methyl-benzoyl chloride (250 mg, 1.62 mmol) in DCM (10.0 ml) at 0°C and the resulting mixture was stirred for 20 min. The solution was concentrated and DMF (20 ml) was added to the residue and heated at 120°C for 20 min. The product was purified by flash chromatography using 10-20% EA in hex. affording 0.250 g (59% yield over 2 steps) of the title compound. GCMS (M/Z)=222.

[1217] Example 928

[1218] 3-Chloromethyl-5-(3-chloro-phenyl)-[1,2,4]oxadiazole

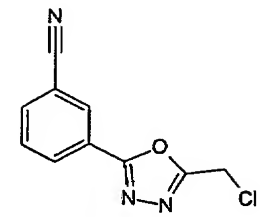


[1219]

[1220] Step A. The acyclic intermediate was obtained from 3-chlorobenzoic acid (2.82 g, 18 mmol), EDCl (3.46 g, 18 mmol), HOBt (2.76 g, 18 mmol) and 2-chloro-N-hydroxy-acetamidine (1.75 g, 16.2 mmol) [Chem. Ber. 1907, 40, 1639] in DMF (40 mL). Step B: The cyclic compound was obtained from heating in DMF (40 mL) and purified by SPE chromatography on silica gel using 2% acetone in hex. yielding the title compound (1.46 g, 39% yield over 2 steps). ^{1}H NMR: 8.17 (m, 1H), 8.07 (dd, 1H), 7.60 (m, 1H), 7.55 (t, 1H), 4.69 (s, 2H).

[1221] Example 929

[1222] 3-[5-(chloromethyl)-1,3,4-oxadiazol-2-yl]benzonitrile

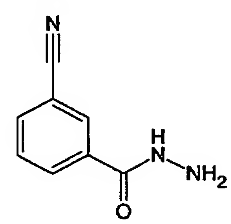


[1223]

[1224] N'-(chloroacetyl)-3-cyanobenzohydrazide (795 mg, 3.34 mmol) and P_2O_5 (4.7 g, 33.4 mmol) were added to DMF (6 ml) and toluene (4 ml). The reaction mixture was refluxed for 2 h. K_2CO_3 (aq., sat.) was added until pH was basic and the mixture was extracted with DCM. The combined organic layers were dried (Na_2SO_4) and purified with flash chromatography using 0 to 100% EA in hep. to give the title compound (209 mg, 29%).^{1}H NMR: 8.29 (m, 2 H), 7.82 (m, 1 H), 7.66 (t, 1 H), 4.78 (s, 2 H).

[1225] Example 930

[1226] 3-cyanobenzohydrazide

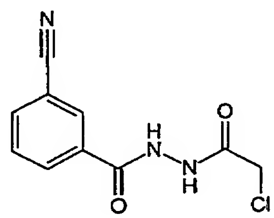


[1227]

[1228] 3-cyanobenzoyl chloride (4.8 g, 29.0 mmol) was dissolved in DCM (20 ml) and MeOH (40 ml) was added in portions at 0°C. The mixture was stirred at 0°C for 1 h and at rt for 2 h. The solvents were evaporated and the crude methyl ester was dissolved in EtOH (50 ml) and hydrazine (24% aq., 9 ml, 45 mmol) was added. The reaction mixture was refluxed for 48 h and the solvents were evaporated (coevaporation with water). The residue was purified with prep. HPLC to give the title compound (1.8 g, 39%). ^{1}H NMR (DMSO-d6): 9.98 (br s, 1 H), 8.21 (m, 1 H), 8.13 (m, 1 H), 7.99 (m, 1 H), 7.69 (t, 1 H), 4.61 (br s, 2 H).

[1229] Example 931

[1230] *N'*-(chloroacetyl)-3-cyanobenzohydrazide

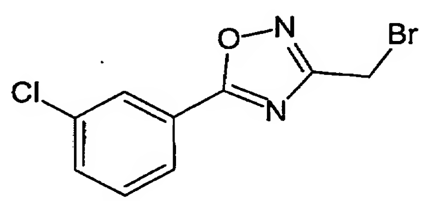


[1231]

[1232] 3-cyanobenzohydrazide (1.6 g, 10.0 mmol) was added to THF (40 ml) and DMF (10 ml). TEA (1.4 ml, 10.0 mmol) was added at 0°C followed by chloroacetyl chloride (1.0 ml, 12.6 mmol) and the reaction mixture was stirred at 0°C for 1 h and at rt for 2 h. The THF was evaporated, water was added to the remaining mixture, followed by filtratation over celite and purification with prep. HPLC to give the title compound (1.6 g, 69%). ^{1}H NMR (DMSO-d6): 10.62 (br s, 2 H), 8.28 (m, 1 H), 8.18 (m, 1 H), 8.08 (m, 1 H), 7.75 (t, 1 H), 4.22 (s, 2 H).

[1233] Example 932

[1234] 3-(bromomethyl)-5-(3-chlorophenyl)-1,2,4-oxadiazole

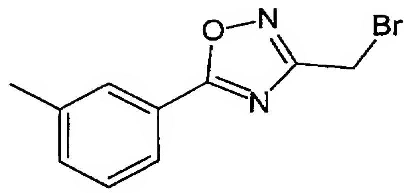


[1235]

[1236] 3-(chloromethyl)-5-(3-chlorophenyl)-1,2,4-oxadiazole (1.38 g, 6.0 mmol) and LiBr (0.90 g, 10.3 mmol) in THF (50 ml) were heated to reflux under a nitrogen atm. o.n. After cooling to r.t. EA was added and the organic phase was washed with H_2O and brine, dried and evaporated to give the title compound (1.40 g, 85%). MS (M^++1) 275.

[1237] Example 933

[1238] 3-(bromomethyl)-5-(3-methylphenyl)-1,2,4-oxadiazole

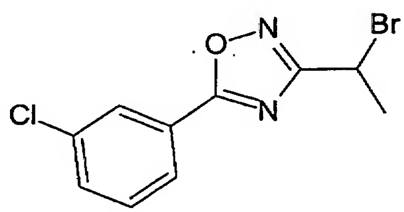


[1239]

[1240] The titel compound was prepared analogous to 3-(bromomethyl)-5-(3-chlorophenyl)-1,2,4-oxadiazole MS (M^{+}+1) 253.

[1241] Example 934

[1242] 3-(1-Bromo-ethyl)-5-(3-chloro-phenyl)-[1,2,4]oxadiazole

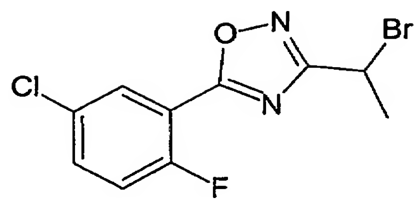


[1243]

[1244] A solution of NBS (396 mg, 2.22 mmol) in THF (2 ml) was added dropwise to a solution of triphenylphosphine (583 mg, 2.22 mmol) in THF (2 ml) at 0°C. After stirring for 20 min 1-[5-(3-chloro-phenyl)-1,2,4-oxadiazol-3-yl]-ethanol (416 mg, 1.85 mmol) in THF (2 ml) was added. Stirring was continued o.n. at r.t. before the solvent was removed under reduced pressure. Flash chromatography (hep/EA 6:1) afforded 168 mg (32%) of the title compound. ^{1}H NMR: 2.12 (d, 3 H) 5.21 (q, 1 H) 7.47 (t, 1 H) 7.57 (m, 1 H) 8.03 (d, 1 H) 8.15 (s, 1 H)

[1245] Example 936

[1246] 3-(1-bromoethyl)-5-(5-chloro-2-fluorophenyl)-1,2,4-oxadiazole

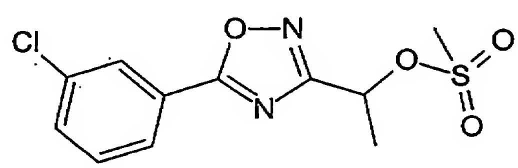


[1247]

[1248] 1.6 g 1-[5-(5-chloro-2-fluorophenyl)-1,2,4-oxadiazol-3-yl]ethanol was dissolved in benzene (30 mL), followed by addition of 0.6 mL phosporous tribromide. After heating to reflux for 90 min water (15 mL) was added. Solid $NaHCO_3$ was added, followed by extraction with $CHCl_3$. After drying over Na_2SO_4 and removal of solvent, purification was done on 2 mm chromatotron plate (hep 100% to hep/EA = 99/1) to yield 0.60 g (32%) of the title compound. ^{1}H NMR: 8.15 (dd, 1 H), 7.49 - 7.59 (m, 1 H), 7.19 - 7.26 (m, 1 H), 5.23 (q, 1 H), 2.13 (d, 3 H)

[1249] Example 937

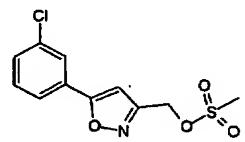
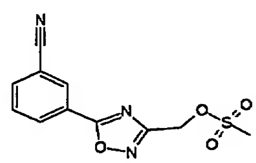
[1250] 1-[5-(3-chlorophenyl)-[1,2,4]oxadiazol-3-yl]ethyl methanesulfonate



[1251]

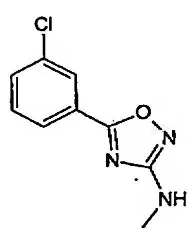
[1252] Methane sulfonyl chloride (40 ml, 0.49 mmol) was added to a mixture of TEA (95 ml, 0.67 mmol) and 1-[5-(3-Chloro-phenyl)-1,2,4-oxadiazol-3-yl]-ethanol (100 mg, 0.45 mmol) in DCM (5 ml). After stirring for 15 min the mixture was washed with water and brine, dried and concentrated to yield the title compound (135 mg). ^{1}H NMR: 1.9 (d, 3 H) 3.1 (s, 3 H) 5.9 (q, 1 H) 7.5 (t, 1 H) 7.6 (m, 1 H) 8.0 (m, 1 H) 8.1 (t, 1 H)

[1253] The following examples were synthesized in a manner analogous to that for 1-[5-(3-chlorophenyl)-[1,2,4]oxadiazol-3-yl]ethyl methanesulfonate.

Structure	Name	^{1}H-NMR	Example No.
	[5-(3-chlorophenyl)isoxazol-3-yl]methyl methanesulfonate	7.80 (s, 1H), 7.70 (m, 1H), 7.45 (m, 2H), 6.73 (s, 1H), 5.37 (s, 2H), 3.16 (s, 3H).	938
	[5-(3-cyanophenyl)-1,2,4-oxadiazol-3-yl]methyl methanesulfonate	(DMSO-d6): 8.56 (m, 1 H), 8.43 (m, 1 H), 8.19 (m, 1 H), 7.85 (m, 1 H), 5.52 (s, 2 H), 3.35 (s, 3 H).	939

[1254] Example 940

[1255] 5-(3-chlorophenyl)-N-methyl-1,2,4-oxadiazol-3-amine



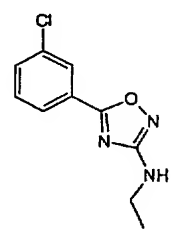
[1256]

[1257] Hydroxycarbonimidic dibromide (2.21 g, 10.89 mmol) was added portionwise over 1 h 20 min to a mixture of 3-chlorobenzonitrile (3.00 g, 21.29 mmol) and $NaHCO_3$ (2.9 g, 34.87 mmol) in toluene (3 ml) at 90 °C. Stirring was continued for 3 h and then the reaction mixture was cooled to r.t., diluted with EA and washed with water. The organic phase was dried and concentrated. A mixture of 3-chlorobenzonitrile and 3-bromo-5-(3-chlorophenyl)-1,2,4-oxadiazole was obtained

after flash chromatography (hex/EA 10:1). 1.0 g of the mixture was dissolved in $MeNH_2$ (4 ml, 8.5 M in EtOH) and heated in a microwave reactor for 30 min at 60 °C. The volatiles were removed under reduced pressure and the residue was dissolved in water and extracted with $CHCl_3$. The organic phase was dried and concentrated. Recrystallization from EA gave 137 mg of the title compound. ^{1}H NMR: 3.00 (d, 3 H) 4.35 (bs, 1 H) 7.43 (t, 1 H) 7.50 - 7.55 (m, 1 H) 7.92 (d, 1 H) 8.03 (s, 1 H)

[1258] Example 941

[1259] 5-(3-chlorophenyl)-N-ethyl-1,2,4-oxadiazol-3-amine

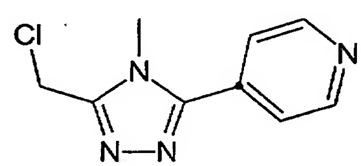


[1260]

[1261] The title compound was prepared analogous to 5-(3-chlorophenyl)-N-methyl-1,2,4-oxadiazol-3-amine. ^{1}H NMR: 1.28 (t, 3 H) 3.36 (q, 2 H) 7.43 (t, 1 H) 7.49 - 7.55 (m, 1 H) 7.92 (m, 1 H) 8.03 (s, 1 H)

[1262] Example 942

[1263] 4-[5-(chloromethyl)-4-methyl-4H-1,2,4-triazol-3-yl]pyridine



[1264]

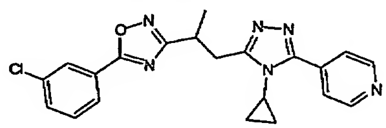
[1265] Sulfuryl dichloride (0.58 ml, 8.34 mmol) in DCM (8 ml) was slowly added to a cooled (-10 °C) solution of 4-(4,5-dimethyl-4H-1,2,4-triazol-3-yl)pyridine (454 mg, 2.61 mmol) in DCM (25 ml) and DMF (8 ml) and then the solution was stirred for 2 h. NaHCO3 (sat.) was added and the mixture was extracted with EA. The organic phase was dried and concentrated. Recrystallization from EA afforded 124

mg (23%) of the title compound. ^{1}H NMR: 3.83 (s, 3 H) 4.84 (s, 2 H) 7.62 (d, 2 H) 8.82 (d, 2 H).

[1266] Preparation of final compounds

[1267] Example 943

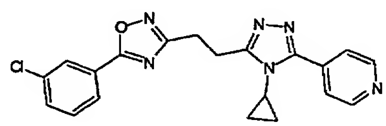
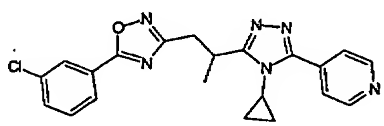
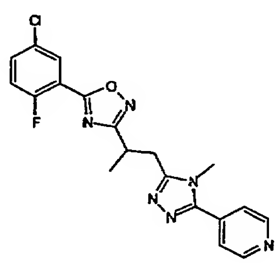
[1268] 4-(5-{2-[5-(3-chlorophenyl)-1,2,4-oxadiazol-3-yl]propyl}-4-cyclopropyl-4*H*-1,2,4-triazol-3-yl)pyridine

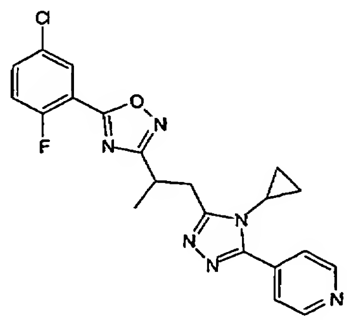
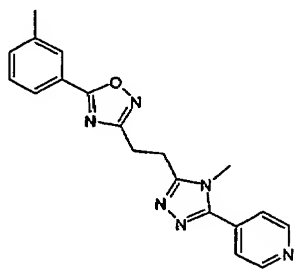
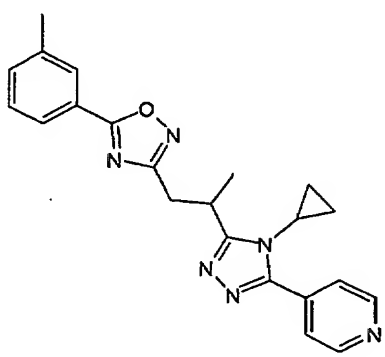
[1269] 

[1270] n-BuLi (210 ml, 2.5 M in hex., 0.52 mmol) was added dropwise to a solution of 4-(4-cyclopropyl-5-methyl-4H-1,2,4-triazol-3-yl)pyridine (80 mg, 0.4 mmol) in THF (10 ml) at -78°C under an atm. of nitrogen. After stirring for 15 min 3-(1-Bromo-ethyl)-5-(3-chloro-phenyl)-[1,2,4]oxadiazole (115 mg, 0.4 mmol) in THF (2 ml) was added. The mixture was stirred for 2 h at -78°C and then at r.t. for 1 h. The solvent was removed under reduced pressure and the desired product was obtained by prep. HPLC in 20 mg yield. ^{1}H NMR: 0.7 (m, 2 H) 1.2 (ddd, 2 H) 1.6 (d, 3 H) 3.2 (dd, 1 H) 3.3 (ddd, 1 H) 3.6 (dd, 1 H) 3.9 (m, 1 H) 7.5 (t, 1 H) 7.6 (m, 1 H) 7.7 (m, 2 H) 8.0 (m, 1 H) 8.1 (t, 1 H) 8.7 (m, 2 H)

[1271] The following examples were synthesized in a manner analogous to that for 4-(5-{2-[5-(3-chlorophenyl)-1,2,4-oxadiazol-3-yl]propyl}-4-cyclopropyl-4*H*-1,2,4-triazol-3-yl)pyridine.

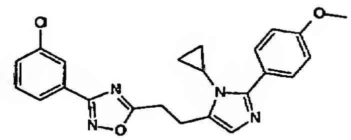
Structure	Example No.	Name	^{1}H-NMR

	944	4-(5-{2-[5-(3-chlorophenyl)-1,2,4-oxadiazol-3-yl]ethyl}-4-cyclopropyl-4*H*-1,2,4-triazol-3-yl)pyridine	0.72 - 0.78 (m, 2 H) 1.21 (m, 2 H) 3.35 (m, 1 H) 3.41 - 3.48 (m, 2 H) 3.49 - 3.57 (m, 2 H) 7.47 (m, 1 H) 7.53 - 7.59 (m, 1 H) 7.73 (m, 2 H) 7.95 - 8.03 (m, 1 H) 8.11 (tm, 1 H) 8.76 (d, 2 H).
	945	4-(5-{2-[5-(3-chlorophenyl)-1,2,4-oxadiazol-3-yl]-1-methylethyl}-4-cyclopropyl-4H-1,2,4-triazol-3-yl)pyridine	0.62 - 0.72 (m, 1 H) 0.81 - 0.92 (m, 1 H) 1.14 - 1.21 (m, 2 H) 1.52 (d, 3 H) 3.24 (m, 1 H) 3.35 (m, 1 H) 3.56 (m, 1 H) 3.83 - 3.93 (m, 1 H) 7.41 (t, 1 H) 7.50 (m, 1 H) 7.68 (d, 2 H) 7.91 (d, 1 H) 8.01 (t, 1 H) 8.70 (d, 2 H)
	946	4-(5-{2-[5-(5-chloro-2-fluorophenyl)-1,2,4-oxadiazol-3-yl]propyl}-4-methyl-4H-1,2,4-triazol-3-yl)pyridine	1.58 (d, 3 H) 3.17 (m, 1 H) 3.38 (m, 1 H) 3.72 (s, 3 H) 3.82 - 3.93 (m, 1 H) 7.20 (t, 1 H) 7.52 (m, 1 H) 7.59 (d, 2 H) 8.07 (m, 1 H) 8.77 (s, 2 H)

	947	4-(5-{2-[5-(5-chloro-2-fluorophenyl)-1,2,4-oxadiazol-3-yl]propyl}-4-cyclopropyl-4H-1,2,4-triazol-3-yl)pyridine	0.69 - 0.81 (m, 2 H) 1.15 - 1.27 (m, 2 H) 1.59 (d, 3 H) 3.23 (m, 1 H) 3.38 (m, 1 H) 3.57 (m, 1 H) 3.92 - 4.03 (m, 1 H) 7.20 (t, J=9.35 Hz, 1 H) 7.52 (m, 1 H) 7.77 (d, 2 H) 8.07 (m, 1 H) 8.76 (d, 2 H)
	948	4-(4-methyl-5-{2-[5-(3-methylphenyl)-1,2,4-oxadiazol-3-yl]ethyl}-4H-1,2,4-triazol-3-yl)pyridine	2.41 (s, 3 H) 3.28 - 3.37 (m, 2 H) 3.44 - 3.52 (m, 2 H) 3.72 (s, 3 H) 7.38 (m, 2 H) 7.61 (d, 2 H) 7.85 - 7.90 (m, 1 H) 7.90 (s, 1 H) 8.78 (bs, 2 H)
	949	4-(4-cyclopropyl-5-{1-methyl-2-[5-(3-methylphenyl)-1,2,4-oxadiazol-3-yl]ethyl}-4H-1,2,4-triazol-3-yl)pyridine	0.69 (m, 1 H) 0.87 (m, 1 H) 1.14 - 1.24 (m, 2 H) 1.55 (d, 3 H) 2.40 (s, 3 H) 3.26 (m, 1 H) 3.35 (m, 1 H) 3.57 (m, 1 H) 3.85 - 3.95 (m, 1 H) 7.37 (d, 2 H) 7.73 (m, 2 H) 7.81 - 7.89 (m, 2 H) 8.73 (bs, 2 H)

[1272] Example 950

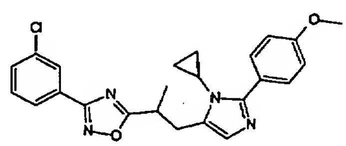
[1273] 3-(3-Chloro-phenyl)-5-{2-[3-cyclopropyl-2-(4-methoxy-phenyl)-3H-imidazol-4-yl]-ethyl}-[1,2,4]oxadiazole

[1274] 

[1275] 3-chloro-N'-hydroxybenzenecarboximidamide (54.3 mg, 0.32 mmol), 3-[3-cyclopropyl-2-(4-methoxy-phenyl)-3H-imidazol-4-yl]-propionic acidethyl ester (100 mg, 0.32 mmol) and sodium-*tert*-butoxide (30.6 mg, 0.32 mmol) were mixed with EtOH (1 ml) and toluene (1 ml), followed by stirring at 100°C for 24h. The mixture was then concentrated, *in-vacuo*, and the residue was purified via column chromatography using 50% EA in hex. and then triturated with Et_2O to isolate the title compound (27 mg). ^{1}H-NMR: 8.1 (m, 1H), 7.97 (dd, 1H), 7.64 (d, 2H), 7.47 (m, 2H), 6.96 (d, 2H), 6.88 (s, 1H), 3.87 (s, 3H), 3.37 (m, 4H), 3.24 (m, 1H), 1.06 (m, 2H), 0.68 (m, 2H).

[1276] Example 951

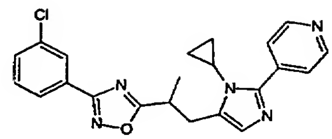
[1277] 3-(3-Chloro-phenyl)-5-{2-[3-cyclopropyl-2-(4-methoxy-phenyl)-3H-imidazol-4-yl]-1-methyl-ethyl}-[1,2,4]oxadiazole

[1278] 

[1279] The title compound was synthesized analogous to 3-(3-Chloro-phenyl)-5-{2-[3-cyclopropyl-2-(4-methoxy-phenyl)-3H-imidazol-4-yl]-ethyl}-[1,2,4]oxadiazole. ^{1}H-NMR: 8.1 (m, 1H), 7.98 (dd, 1H), 7.63 (d, 2H), 7.46 (m, 2H), 6.97 (d, 2H), 6.85 (s, 1H), 3.88 (s, 3H), 3.65 (m, 1H), 3.42 (m, 1H), 3.15 (m, 2H), 1.58 (d, 3H), 1.06 (m, 2H), 0.67 (m, 2H).

[1280] Example 952

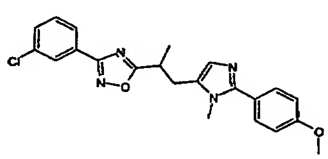
[1281] 4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propyl}-1-cyclopropyl-1H-imidazol-2-yl)-pyridine

[1282] 

[1283] 3-chloro-N-hydroxy-benzamidine (486 mg, 2.85 mmol), 3-(3-cyclopropyl-2-pyridin-4-yl-3H-imidazol-4-yl)-2-methyl-propionic acid (702 mg, 2.59 mmol), EDCl (546 mg, 2.85 mmol) and HOBt hydrate (385 mg, 2.85 mmol) were mixed with DMF (20 ml) and stirred o.n. at r.t. The reaction was diluted with water and extracted with EA. The combined organic phase was successively washed with sat. aq. sodium bicarbonate, brine, dried (Na_2SO_4), filtered and concentrated *in-vacuo*. The residue was heated in DMF (10 ml) at 120°C for 2 h. The reaction mixture was cooled to r.t., diluted with EA (50 ml), successively washed with water and brine, dried (Na_2SO_4), filtered and concentrated *in-vacuo*. The crude was purified via column chromatography using 2% MeOH in DCM to isolate the title compound (404 mg). ^{1}H-NMR: 8.69 (dd, 2H), 8.09 (m, 1H), 7.96 (d, 1H), 7.67 (dd, 2H), 7.46 (m, 2H), 6.94 (s, 1H), 3.66 (m, 1H), 3.48 (m, 1H), 3.31 (m, 1H), 3.16 (m, 1H), 1.59 (d, 3H), 1.19 (m, 2H), 0.72 (m, 2H).

[1284] Example 953

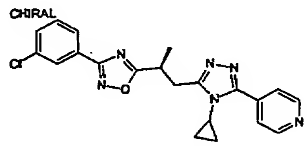
[1285] 3-(3-Chloro-phenyl)-5-{2-[2-(4-methoxy-phenyl)-3-methyl-3H-imidazol-4-yl]-1-methyl-ethyl}-[1,2,4]oxadiazole

[1286] 

[1287] The title compound was synthesized analogous to 4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propyl}-1-cyclopropyl-1H-imidazol-2-yl)-pyridine. ^{1}H-NMR: 8.1 (m, 1H), 7.98 (dd, 1H), 7.50 (m, 4H), 6.97 (d, 2H), 6.92 (s, 1H), 3.87 (s, 3H), 3.62 (s, 3H) 3.54 (m, 1H), 3.30 (m, 1H), 3.00 (m, 1H), 1.57 (d, 3H).

[1288] Example 954

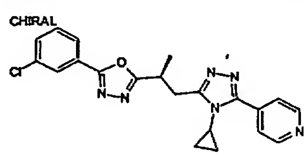
[1289] (S)-4-(5-{2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine

[1290] 

[1291] After 3-chloro-N-hydroxy-benzamidine (0.7 g, 4.1 mmol) was mixed with potassium-*tert*-butoxide (0.373 g, 3.33 mmol) in n-propanol at 80 °C for 10 min, 3-(4-cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-yl)-2-methyl-propionic acid ethyl ester (1.0g, 3.33 mmol) was added to the reaction mixture and heated at 100 °C for 3 h. The reaction mixture was concentrated, quenched with sat. ammonium chloride and extracted with DCM. The organic layer was dried with $MgSO_4$, purified by column chromatography and triturated with Et_2O to give racemic 4-(5-{2-[3-(3-chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propyl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine (0.8g, 59%). The title product (10mg) was obtained by separation on Chiracel OJ with EtOH:hex. (1:4). ^{1}H-NMR: 8.78(d, 2H), 8.05 (s, 1H), 7.96 (d, 1H), 7.74 (d, 2H), 7.50 (d, 1H), 7.43 (t, 1H), 4.15 (m, 1H), 3.64 (dd, 1H), 3.31 (m, 2H), 1.67 (d, 3H), 1.25 (m, 2H) and 0.78 (m, 2H).

[1292] Example 955

[1293] 4-(5-{(2S)-2-[5-(3-chlorophenyl)-1,3,4-oxadiazol-2-yl]propyl}-4-cyclopropyl-4H-1,2,4-triazol-3-yl)pyridine

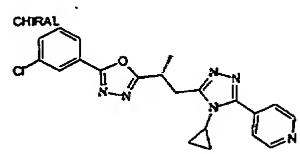
[1294] 

[1295] 3-(4-cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-yl)-2-methyl-propionic acid ethyl ester (2.14 g, 7.1 mmol) was mixed with hydrazine monohydrate in ethanol at 120 °C in a sealed flask for 2 hours. The reaction mixture was concentrated and triturated with ether to give 3-(4-cyclopropyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-yl)-2-methyl-propionic acid hydrazide. This compound was mixed with 3-Chloro-

benzimidic acid ethyl ester hydrochloride (0.722 g, 7.8 mmol) in ethanol at 130 °C o.n.. The reaction mixture was concentrated, quenched with saturated sodium carbonate, extracted with DCM. The organic layer was dried and purified by column chromatograph with 5 % methanol (2M NH_3) in DCM to racemic 4-(5-{2-[3-(3-chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-propyl}-4-cyclopropyl-4H[1,2,4] triazol-3-yl)-pyridine 1.19 g (41.1 %). This material (70 mg) was separated on Chiralpak AD using ethanol as eluent to give the title compound. ^{1}H-NMR: 8.77(d, 2H), 8.02 (s, 1H), 7.92 (d, 1H), 7.72 (d, 2H), 7.51 (d, 1H), 7.47(t, 1H), 4.12 (m, 1H), 3.69 (dd, 1H), 3.44 (m, 1H), 3.26 (dd, 1H), 1.66 (d, 3H), 1.24 (m, 2H) and 0.79 (m, 2H).

[1296] Example 956

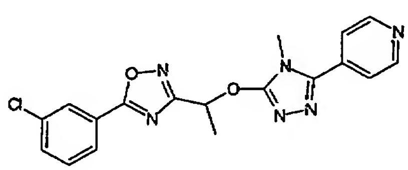
[1297] 4-(5-{(2R)-2-[5-(3-chlorophenyl)-1,3,4-oxadiazol-2-yl]propyl}-4-cyclopropyl-4H-1,2,4-triazol-3-yl)pyridine

[1298] 

[1299] The title compound was obtained from chiral LC separation in example 4-(5-{(2S)-2-[5-(3-chlorophenyl)-1,3,4-oxadiazol-2-yl]propyl}-4-cyclopropyl-4H-1,2,4-triazol-3-yl)pyridine.

[1300] Example 957

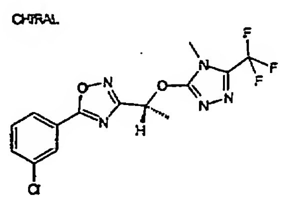
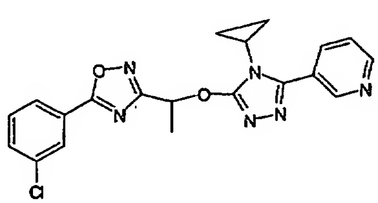
[1301] 4-(5-{1-[5-(3-chlorophenyl)-1,2,4-oxadiazol-3-yl]ethoxy}-4-methyl-4H-1,2,4-triazol-3-yl)pyridine

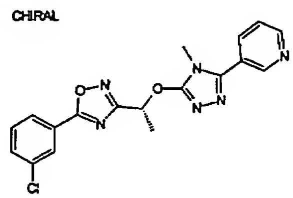
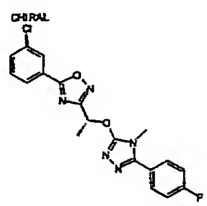
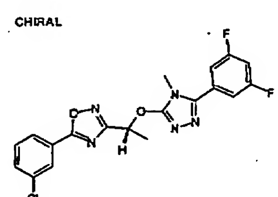
[1302] 

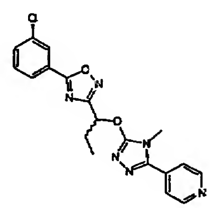
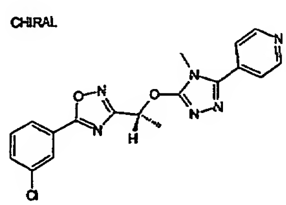
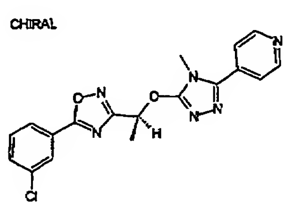
[1303] 1.45 g (6.08 mmol) 4-[4-Methyl-5-(methylsulfonyl)-4H-1,2,4-triazol-3-yl]pyridine, 1.73 g (7.70 mmol) 1-[5-(3-chlorophenyl)-1,2,4-oxadiazol-3-yl]ethanol and 4.03 g (12.3 mmol) cesium carbonate were dissolved under Ar-atmosphere in

DMF (25 mL) and stirred at 30°C for 3 d. After filtration and evaporation to dryness the crude was purified on 4mm silica chromatotron plate (DCM/MeOH = 100/0 to 90/10). Further purification on 2 mm silica chromatotron plate (Hep/EA/MeOH = 15/15/1) gave 0.36 g (15%) of the title compound. ^{1}H NMR: 8.75 (br s, 2 H), 8.12 (s, 1 H), 8.00 (d, 1 H), 7.64 (d, 2 H), 7.56 (d, 1 H), 7.46 (t, 1 H), 6.39 (q, 1 H), 3.63 (s, 3 H), 1.94 (d, 3 H).

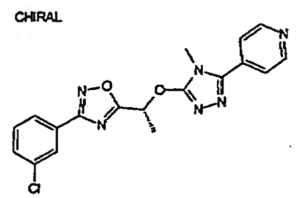
[1304] The following examples were synthesized analogous to 4-(5-{1-[5-(3-chlorophenyl)-1,2,4-oxadiazol-3-yl]ethoxy}-4-methyl-4H-1,2,4-triazol-3-yl)pyridine.

Structure	Example No.	Name	^{1}H-NMR
	958	5-(3-chlorophenyl)-3-((1R)-1-{[4-methyl-5-(trifluoromethyl)-4H-1,2,4-triazol-3-yl]oxy}ethyl)-1,2,4-oxadiazole	8.13 (m, 1 H) 8.01 (m, 1 H) 7.58 (m, 1 H) 7.48 (m, 1 H) 6.24 (q, 1 H) 3.74 (s, 3 H) 1.90 (d, 3 H).
	959	3-(5-{1-[5-(3-chlorophenyl)-1,2,4-oxadiazol-3-yl]ethoxy}-4-cyclopropyl-4H-1,2,4-triazol-3-yl)pyridine	1.04 (m, 4H) 1.96 (d, 3H) 3.21 (m, 1H) 6.41 (q, 1H) 7.45 (m, 2H) 7.58 (m, 1H) 8.03 (d, 1H) 8.15 (m, 2H) 8.70 (bd, 1H) 9.08 (bs, 1H)

	**960**	3-(5-{(1*R*)-1-[5-(3-chlorophenyl)-1,2,4-oxadiazol-3-yl]ethoxy}-4-methyl-4*H*-1,2,4-triazol-3-yl)pyridine	1.95 (d, 3H) 3.59 (s, 3H) 6.39 (q, 1H) 7.46 (m, 1H) 7.49 (t, 1H) 7.58 (m, 1H) 8.02 (m, 2H) 8.14 (t, 1H) 8.72 (bd, 1H) 8.89 (bs, 1H)
	**961**	5-(3-chlorophenyl)-3-((1R)-1-{[5-(4-fluorophenyl)-4-methyl-4H-1,2,4-triazol-3-yl]oxy}ethyl)-1,2,4-oxadiazole	8.14 (m, 1 H) 8.02 (m, 1 H) 7.93 - 7.99 (m, 2 H) 7.57 (m, 1 H) 7.47 (m, 1 H) 7.06 (m, 2 H) 6.30 (q, 1 H) 3.71 (s, 3 H) 1.90 (d, 3 H).
	**962**	5-(3-chlorophenyl)-3-((1*R*)-1-{[5-(3,5-difluorophenyl)-4-methyl-4*H*-1,2,4-triazol-3-yl]oxy}ethyl)-1,2,4-oxadiazole	1.93 (d, 3 H) 3.57 (s, 3 H) 6.37 (m, 1 H) 6.86 - 6.97 (m, 1 H) 7.20 (d, 2 H) 7.46 (t, 1 H) 7.56 (d, 1 H) 8.00 (d, 1 H) 8.12 (s, 1 H)

	**963**	(+)-4-(5-{1-[5-(3-chlorophenyl)-1,2,4-oxadiazol-3-yl]propoxy}-4-methyl-4*H*-1,2,4-triazol-3-yl)pyridine	1.12 (t, 3 H) 2.25 - 2.36 (m, 2 H) 3.64 (s, 3 H) 6.22 (t, J=6.57 Hz, 1 H) 7.46 (t, 1 H) 7.54 - 7.63 (m, 3 H) 7.97 - 8.05 (m, 1 H) 8.12 (t, 1 H) 8.70 - 8.78 (m, 2 H).
	**964**	(-)-4-(5-{(1R)-1-[5-(3-chlorophenyl)-1,2,4-oxadiazol-3-yl]ethoxy}-4-methyl-4H-1,2,4-triazol-3-yl)pyridine	8.74 (d, 2 H), 8.13 (t, 1 H), 8.01 (d, 1 H), 7.60 (dd, 2 H), 7.57 (d, 1 H), 7.47 (t, 1 H), 6.39 (q, 1 H), 3.63 (s, 3 H), 1.94 (d, 3 H).
	**965**	(+)-4-(5-{(1S)-1-[5-(3-chlorophenyl)-1,2,4-oxadiazol-3-yl]ethoxy}-4-methyl-4H-1,2,4-triazol-3-yl)pyridine	8.71 (d, 2 H), 8.09 (s, 1 H), 7.97 (d, 1 H), 7.57 (d, 2 H), 7.54 (d, 1 H), 7.44 (t, 1 H), 6.36 (q, 1 H), 3.60 (s, 3 H), 1.91 (d, 3 H).

[1306] (-)-4-(5-{1-[3-(3-chlorophenyl)-1,2,4-oxadiazol-5-yl]ethoxy}-4-methyl-4H-1,2,4-triazol-3-yl)pyridine

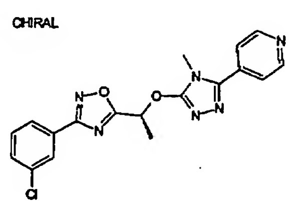


[1307]

[1308] 0.57 g (2.54 mmol) (+)-(1R)-1-[3-(3-chlorophenyl)-1,2,4-oxadiazol-5-yl]ethanol, 0.64 g (2.68 mmol) 4-[4-methyl-5-(methylsulfonyl)-4H-1,2,4-triazol-3-yl]pyridine and 0.90 g (2.76 mmol) cesium carbonate were stirred at 65°C for 6 h, followed by dilution with water. Extraction with EA, washing with aq. citric acid, drying over Na_2SO_4, followed by purification via chromatotron 2mm (Hep/EA/MeOH=10/10/1) gave 0.81 g (83%) racemic 4-(5-{1-[3-(3-chlorophenyl)-1,2,4-oxadiazol-5-yl]ethoxy}-4-methyl-4H-1,2,4-triazol-3-yl)pyridine. Prep. chiral separation on Chiralpak AD using 100% 2-propanol yielded 0.25 g of the title compound as the second eluting enantiomer. ^{1}H NMR: 8.76 (d, 2 H), 8.07 (t, 1 H), 7.92 - 7.99 (m, 1 H), 7.60 - 7.68 (m, 2 H), 7.45 - 7.51 (m, 1 H), 7.41 (t, 1 H), 6.45 (q, 1 H), 3.66 (s, 3 H), 1.99 (d, 3 H)

[1309] Example 967

[1310] (+)-4-(5-{1-[3-(3-chlorophenyl)-1,2,4-oxadiazol-5-yl]ethoxy}-4-methyl-4H-1,2,4-triazol-3-yl)pyridine



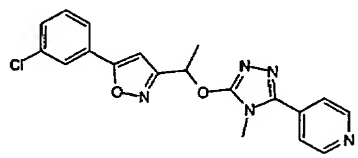
[1311]

[1312] 0.2 g of the title compound was isolated as the first eluting enantiomer during preparative chiral HPLC separation in the example of (-)-4-(5-{1-[3-(3-chlorophenyl)-1,2,4-oxadiazol-5-yl]ethoxy}-4-methyl-4H-1,2,4-triazol-3-yl)pyridine. ^{1}H NMR: 8.77 (d, 2 H), 8.07 (t, 1 H), 7.93 - 8.00 (m, 1 H), 7.68 (dd, 2 H), 7.45 - 7.52

(m, 1 H), 7.41 (t, 1 H), 6.45 (q, 1 H), 3.67 (s, 3 H), 1.99 (d, 3 H)

[1313] Example 968

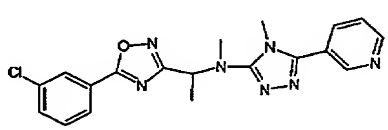
[1314] 4-(5-{1-[5-(3-Chloro-phenyl)-isoxazol-3-yl]-ethoxy}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine

[1315] 

[1316] 1-[5-(3-chloro-phenyl)-isoxazol-3-yl]-ethanol (63.4 mg, 0.28 mmol), DMF and sodium hydride (60% dispersion in oil, 15.1 mg, 0.38 mmol) were mixed under inert atm. and stirred at r.t for 1 h, followed by addition of 4-[4-methyl-5-(methylsulfonyl)-4H-1,2,4-triazol-3-yl]pyridine (45 mg, 0.19 mmol). After stirring at 80°C for 24h, the mixture was cooled to r.t., diluted with EA, sequentially washed with water and brine. The organic phase was dried (Na_2SO_4), filtered and concentrated, *in-vacuo*. The crude residue was purified via column chromatagraphy using 5% MeOH in EA to isolate the title compound (11.7 mg). ^{1}H-NMR: 8.81 (bs, 2H), 7.77 (s, 1H), 7.67 (m, 3H), 7.42 (m, 2H), 6.73 (s, 1H), 6.36 (q, 1H), 3.62 (s, 3H), 1.94 (d, 3H).

[1317] Example 969

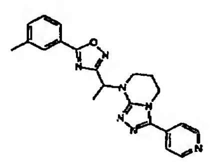
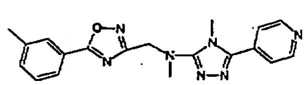
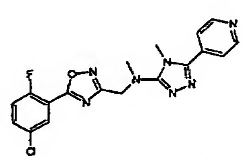
***[1318]* *N*-{1-[5-(3-chlorophenyl)-1,2,4-oxadiazol-3-yl]ethyl}-*N*,4-dimethyl-5-pyridin-3-yl-4*H*-1,2,4-triazol-3-amine**

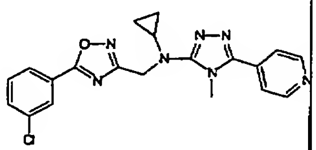
[1319] 

[1320] NaH (14 mg, 0.35 mmol) was added to N,4-dimethyl-5-pyridin-3-yl-4H-1,2,4-triazol-3-amine (33 mg, 0.18 mmol) in DMF (3 mL). After 30 min 3-(1-chloroethyl)-5-(3-chlorophenyl)-1,2,4-oxadiazole (80 mg, 0.18 mmol) in DMF (1 mL) was added to the mixture and the reaction was stirred at 60 °C o.n. Brine was added

and the mixture was extracted with EA. The organic phase was dried and concentrated. The product was purified by column chromatography (DCM to DCM-MeOH 30:1) to give 31 mg (43%) of the title compound. ^{1}H NMR: 1.71 (d, 3H) 2.97 (s, 3H) 3.67 (s, 3H) 4.88 (q, 1H) 7.46 (m, 2H) 7.56 (d, 1H) 8.00 (d, 1H) 8.10 (d, 2H) 8.71 (bs, 1H) 8.92 (bs, 1H)

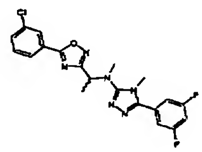
[1321] The following examples were made in a manner analogous to that for *N*-{1-[5-(3-chlorophenyl)-1,2,4-oxadiazol-3-yl]ethyl}-*N*,4-dimethyl-5-pyridin-3-yl-4*H*-1,2,4-triazol-3-amine.

Structure	Example No.	Name	^{1}H-NMR
	970	3-Pyridin-4-yl-8-[1-(5-m-tolyl-[1,2,4]oxadiazol-3-yl)-ethyl]-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrimidine	1.76 (d, 3 H) 2.18 (m, 2H) 2.44 (s, 3H) 3.46 (t, 2H) 4.15 (m, 2 H) 5.99 (q, 2 H) 7.40 (d, 2 H) 7.62 (d, 2 H) 7.89 (d, 1 H) 7.90 (s, 1 H) 8.70 (d, 2 H).
	971	*N*,4-dimethyl-*N*-{[5-(3-methylphenyl)-1,2,4-oxadiazol-3-yl]methyl}-5-pyridin-4-yl-4*H*-1,2,4-triazol-3-amine	2.43 (s, 3H) 3.08 (s, 3H) 3.71 (s, 3H) 4.56 (s, 2H) 7.40 (d, 2H) 7.66 (d, 2H) 7.92 (m, 2H) 8.77 (bs, 2H)
	972	*N*-{[5-(5-chloro-2-fluorophenyl)-1,2,4-oxadiazol-3-yl]methyl}-*N*,4-dimethyl-5-pyridin-4-yl-4*H*-1,2,4-triazol-3-amine	3.04 (s, 3H) 3.66 (s, 3H) 4.56 (s, 2H) 7.19 (m, 1H) 7.49 (m, 1H) 7.64 (bs, 2H) 8.03 (m, 1H) 8.72 (bs, 2H)

	973	*N*-{[5-(4-chlorophenyl)-1,2,4-oxadiazol-3-yl]methyl}-*N*-cyclopropyl-4-methyl-5-pyridin-4-yl-4*H*-1,2,4-triazol-3-amine	1H NMR: 0.6 (s, 2 H) 0.8 (d, 2 H) 3.1 (s, 1 H) 3.7 (s, 3 H) 4.7 (s, 2 H) 7.4 (t, 1 H) 7.5 (d, 1 H) 7.6 (d, 2 H) 7.9 (d, 1 H) 8.1 (s, 1 H) 8.7 (s, 2 H)

[1322] Example 974

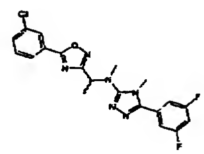
[1323] (+)-*N*-{1-[5-(3-chlorophenyl)-1,2,4-oxadiazol-3-yl]ethyl}-5-(3,5-difluorophenyl)-*N*,4-dimethyl-4*H*-1,2,4-triazol-3-amine

[1324] 

[1325] To a solution of 5-(3,5-difluorophenyl)-N,4-dimethyl-4H-1,2,4-triazol-3-amine (0.47 g, 2.10 mmol) in DMF (10 ml) at r.t. under nitrogen was added NaH (77 mg, 3.20 mmol).After stirring for 15 min. a solution of 1-[5-(3-chlorophenyl)-1,2,4-oxadiazol-3-yl]ethyl methanesulfonate (0.70 g, 2.30 mmol) in DMF 10 ml was added. After 3 h the mixture was diluted with sat. NH_4Cl solution and then extracted with EA. The organic phase was washed with H_2O and brine, dried and evaporated. Purification by silica gel chromatography using hex.:EA=1:1 afforded 400 mg of the racemic N-{1-[5-(3-chlorophenyl)-1,2,4-oxadiazol-3-yl]ethyl}-5-(3,5-difluorophenyl)-N,4-dimethyl-4H-1,2,4-triazol-3-amine, which was separated using prep. chiral HPLC on a Chiralpak AD column (hex./2-propanol 80/20 to 100% 2-propanol) to give 183 mg (21%) of the title compound which eluted last. ^{1}H NMR: 1.68 (d, 3 H) 2.89 (s, 3 H) 3.62 (s, 3 H) 4.79 (q, 1 H) 6.80 - 6.90 (m, 1 H) 7.19 (d, 2 H) 7.40 (t, 1 H) 7.49 (d, 1 H) 7.94 (d, 1 H) 8.04 (s, 1 H)

[1326] Example 975

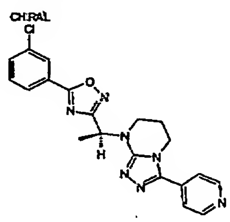
[1327] (-)-*N*-{1-[5-(3-chlorophenyl)-1,2,4-oxadiazol-3-yl]ethyl}-5-(3,5-difluorophenyl)-*N*,4-dimethyl-4*H*-1,2,4-triazol-3-amine

[1328] 

[1329] 186 mg of the title compound was isolated as the first eluting enantiomer during preparative chiral HPLC separation in example of (+)-N-{1-[5-(3-chlorophenyl)-1,2,4-oxadiazol-3-yl]ethyl}-5-(3,5-difluorophenyl)-N,4-dimethyl-4H-1,2,4-triazol-3-amine. ^{1}H NMR: 1.68 (d, 3 H) 2.89 (s, 3 H) 3.62 (s, 3 H) 4.79 (q, 1 H) 6.80 - 6.90 (m, 1 H) 7.19 (d, 2 H) 7.40 (t, 1 H) 7.49 (d, 1 H) 7.94 (d, 1 H) 8.04 (s, 1 H).

[1330] Example 976

[1331] (+)-8-{(1S)-1-[5-(3-chlorophenyl)-1,2,4-oxadiazol-3-yl]ethyl}-3-pyridin-4-yl-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyrimidine

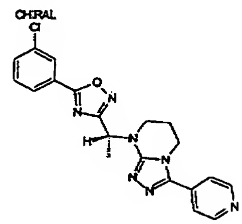
[1332] 

[1333] NaH (716 mg, 29.8 mmol) was added slowly to a solution of 3-pyridin-4-yl-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyrimidine (5.0 g, 24.8 mmol) in DMF (250 ml) under nitrogen. After 10 min a solution of 3-(1-chloroethyl)-5-(3-chlorophenyl)-1,2,4-oxadiazole (6.0 g, 24.8 mmol) in DMF (200 ml) was added, followed by stirring o.n. at r.t.. A sat NH_4Cl solution was added followed by water. The mixture was extracted with EA and DCM. The combined organic extracts were washed with water and brine, dried and concentrated. Recrystallization from EA gave 2.24 g (22%) of the racemic product 8-{1-[5-(3-chlorophenyl)-1,2,4-oxadiazol-3-yl]ethyl}-3-pyridin-4-yl-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyrimidine. Separation on a Chiralpak AD column (100% 2-propanol) gave the title compound which eluted as second enantiomer. ^{1}H NMR: 1.74 (d, 3 H) 2.17 (m, 2 H) 3.45 (m, 2 H) 4.10 (m, 2 H) 5.96 (m, 1 H) 7.44 (t, 1 H) 7.53 (m, 1 H) 7.59 (m, 2 H) 7.97 (m, 1 H) 8.08 (m, 1 H) 8.67 (d,

2 H)

[1334] Example 977

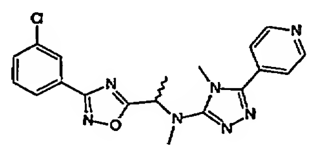
[1335] (-)-8-{(1R)-1-[5-(3-chlorophenyl)-1,2,4-oxadiazol-3-yl]ethyl}-3-pyridin-4-yl-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyrimidine

[1336] 

[1337] The title compound was isolated as the first eluting enantiomer during preparative chiral HPLC separation in example of (+)-8-{(1S)-1-[5-(3-chlorophenyl)-1,2,4-oxadiazol-3-yl]ethyl}-3-pyridin-4-yl-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyrimidine. ^{1}H NMR: 1.74 (d, 3 H) 2.17 (m, 2 H) 3.45 (m, 2 H) 4.10 (m, 2 H) 5.96 (m, 1 H) 7.44 (t, 1 H) 7.53 (m, 1 H) 7.59 (m, 2 H) 7.97 (m, 1 H) 8.08 (m, 1 H) 8.67 (d, 2 H)

[1338] Example 978

[1339] (-)-N-{1-[3-(3-chlorophenyl)-1,2,4-oxadiazol-5-yl]ethyl}-N,4-dimethyl-5-pyridin-4-yl-4H-1,2,4-triazol-3-amine

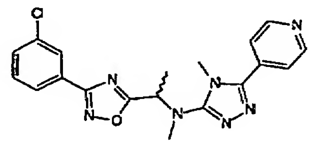
[1340] 

[1341] Prep. chiral HPLC separation on Chiralpak AD (100% 2-propanol) yielded the title compound as the last eluting isomer. ^{1}H NMR: 8.74 (s, 2 H), 8.05 (t, 1 H), 7.87 - 8.00 (m, 1 H), 7.56 - 7.69 (m, 2 H), 7.32 - 7.53 (m, 2 H), 5.03 (q, 1 H), 3.68 (s, 3 H), 2.98 (s, 3 H), 1.81 (d, 3 H)

[1342] Example 979

[1343] (+)-N-{1-[3-(3-chlorophenyl)-1,2,4-oxadiazol-5-yl]ethyl}-N,4-dimethyl-5-

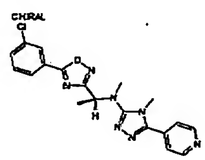
pyridin-4-yl-4H-1,2,4-triazol-3-amine

[1344] 

[1345] Prep. chiral HPLC separation on Chiralpak AD (100% 2-propanol) yielded the title compound as the first eluting isomer. ^{1}H NMR: 8.74 (s, 2 H), 8.05 (t, 1 H), 7.87 - 8.00 (m, 1 H), 7.56 - 7.69 (m, 2 H), 7.32 - 7.53 (m, 2 H), 5.03 (q, 1 H), 3.68 (s, 3 H), 2.98 (s, 3 H), 1.81 (d, 3 H)

[1346] Example 980

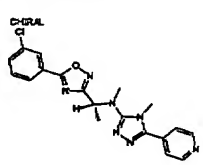
[1347] (-)-N-{(1S)-1-[5-(3-chlorophenyl)-1,2,4-oxadiazol-3-yl]ethyl}-N,4-dimethyl-5-pyridin-4-yl-4H-1,2,4-triazol-3-amine

[1348] 

[1349] Prep. chiral HPLC separation on Chiralpak AD (100% 2-propanol) of racemic N-{1-[5-(3-chlorophenyl)-1,2,4-oxadiazol-3-yl]ethyl}-N,4-dimethyl-5-pyridin-4-yl-4H-1,2,4-triazol-3-amine yielded the title compound which eluted last.

[1350] Example 981

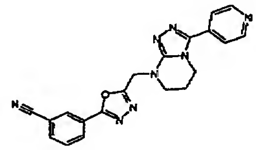
[1351] (+)-N-{(1R)-1-[5-(3-chlorophenyl)-1,2,4-oxadiazol-3-yl]ethyl}-N,4-dimethyl-5-pyridin-4-yl-4H-1,2,4-triazol-3-amine

[1352] 

[1353] The title compound was isolated as the first eluting enantiomer during prep. chiral HPLC separation in example of (-)-N-{(1S)-1-[5-(3-chlorophenyl)-1,2,4-oxadiazol-3-yl]ethyl}-N,4-dimethyl-5-pyridin-4-yl-4H-1,2,4-triazol-3-amine.

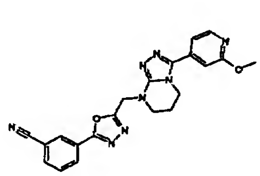
[1354] Example 982

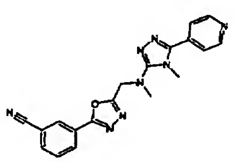
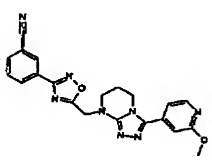
[1355] 3-[5-(3-Pyridin-4-yl-6,7-dihydro-5*H*-[1,2,4]triazolo[4,3-*a*]pyrimidin-8-ylmethyl)[1,3,4]oxadiazol-2-yl]benzonitrile

[1356] 

[1357] 3-pyridin-4-yl-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-*a*]pyrimidine (172 mg, 0.85 mmol) and 3-[5-(chloromethyl)-1,3,4-oxadiazol-2-yl]benzonitrile (94 mg, 0.43 mmol) were dissolved in butanone (5 ml) and K_2CO_3 (118 mg, 0.85 mmol) and KI (35 mg, 0.21 mmol) were added. The reaction mixture was refluxed for 1 h and the solvent was evaporated. The residue was dissolved in K_2CO_3 (aq., 1M, 25 ml) and was extracted with DCM. The combined organic layers were dried (Na_2SO_4) and purified with prep. HPLC to give the title compound (27 mg, 16%). ^{1}H NMR: 8.75 (d, 2H), 8.30 (m, 2H), 7.79 (d, 1H), 7.63 (m, 1H), 7.53 (dd, 2H), 5.57 (d, 2H), 4.06 (t, 2H), 3.58 (t, 2H), 1.99 (m, 2H).

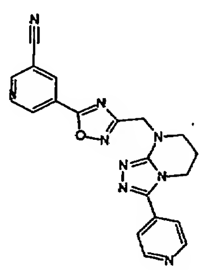
[1358] The following compounds were prepared analogous to 3-[5-(3-Pyridin-4-yl-6,7-dihydro-5*H*-[1,2,4]triazolo[4,3-*a*]pyrimidin-8-ylmethyl)[1,3,4]oxadiazol-2-yl]benzonitrile

Structure	Example No.	Name	^{1}H-NMR
	983	3-{5-[3-(2-Methoxypyridin-4-yl)-6,7-dihydro-5*H*-[1,2,4]triazolo[4,3-*a*]pyrimidin-8-ylmethyl][1,3,4]oxadiazol-2-yl}benzonitrile	8.31 (s, 1H), 8.26 (t, 2H), 7.80 (d, 1H), 7.63 (t, 1H), 7.11 (d, 1H), 6.93 (s, 1H), 5.48 (d, 2H), 4.01 (t, 2H), 3.96 (s, 3H), 3.56 (s, 2H), 1.96 (s, 2H).

	984	3-(5-{[Methyl-(4-methyl-5-pyridin-4-yl-4*H*-[1,2,4]triazol-3-yl)-amino]-methyl}[1,3,4]oxadiazol-2-yl)benzonitrile	8.77 (s, 2H), 8.30 (m, 2H), 7.82 (d, 1H), 7.65 (m, 3H), 4.79 (s, 2H), 3.71 (s, 3H), 3.11 (s, 3H).
	985	3-{5-[3-(2-Methoxy-pyridin-4-yl)-6,7-dihydro-5H-[1,2,4]triazolo[4,3-a]pyrimidin-8-ylmethyl]-[1,2,4]oxadiazol-3-yl}-benzonitrile	8.29 (m, 3 H), 7.77 (d, 1 H), 7.59 (t, 1 H), 6.98 (s, 1 H), 5.11 (s, 2 H), 4.17 (m, 2 H), 3.97 (s, 3 H), 3.63 (m, 2 H), 2.29 (m, 2 H).

[1359] Example 986

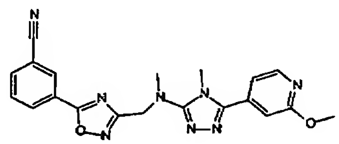
[1360] 3-{3-[(3-pyridin-4-yl-6,7-dihydro[1,2,4]triazolo[4,3-*a*]pyrimidin-8(5*H*)-yl)methyl]-1,2,4-oxadiazol-5-yl}benzonitrile

[1361] 

[1362] [5-(3-cyanophenyl)-1,2,4-oxadiazol-3-yl]methyl methanesulfonate (0.278 g; 0.99 mmol) and 3-pyridin-4-yl-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-*a*]pyrimidine (0.220 g; 1.09 mmol) were dissolved in butanone (20 ml) and potassium carbonate (0.275 g; 1.99 mmol) was added portionwise. The mixture was heated at reflux for 18 h before cooling to r.t.. This mixture was concentrated *in vacuo* and DCM (20 ml) was added. The mixture was washed with water, dried (Na_2SO_4), evaporated and purified using prep. HPLC chromatography to give the title compound (5.4 mg). ^{1}H NMR: 8.77 (m, 2H), 8.41 (s, 1H), 8.34 (d, 1H), 7.87 (d, 1H), 7.68 (t, 1H), 7.56 (m, 2H) 5.51 (s, 2H), 4.09 (m, 2H), 3.62 (m, 2H), 2.19 (m, 2H).

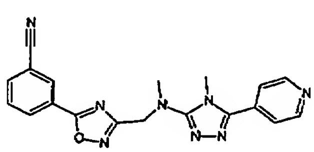
[1363] Example 987

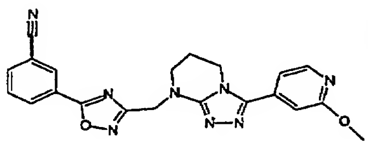
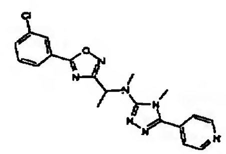
[1364] 3-(3-{[[5-(2-methoxypyridin-4-yl)-4-methyl-4*H*-1,2,4-triazol-3-yl](methyl)amino]methyl}-1,2,4-oxadiazol-5-yl)benzonitrile

[1365] 

[1366] Sodium hydride (0.013 g, 0.53 mmol) was added portionwise to a stirred solution of 5-(2-methoxypyridin-4-yl)-*N*,4-dimethyl-4*H*-1,2,4-triazol-3-amine (0.086 g; 0.39 mmol) in DMF (10 ml) at 0°C. The mixture was stirred for 30 minutes before [5-(3-cyanophenyl)-1,2,4-oxadiazol-3-yl]methyl methanesulfonate (0.1 g; 0.36 mmol) in DMF (1 ml) was added dropwise. The mixture was stirred at r.t. for 3 h before quenching with water (30 ml). The resulting mixture was extracted with EA (3 x 40 ml). The organics were combined, dried (Na_2SO_4) and evaporated to give a crude material, which was purified by prep. HPLC to give the title compound (0.061 g; 42.3%). ^{1}H NMR: 8.49 (s, 1H), 8.33 (dd, 1H), 8.28 (d, 1H), 7.86 (dd, 1H), 7.67 (t, 1H), 7.24 (d, 1H), 7.02 (s, 1H), 4.60 (s, 2H), 3.97 (s, 3H), 3.70 (s, 3H), 3.08 (s, 3H).

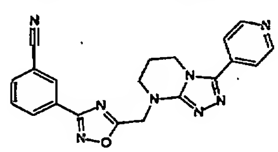
[1367] The following examples were prepared in a manner analogous to that for 3-(3-{[[5-(2-methoxypyridin-4-yl)-4-methyl-4*H*-1,2,4-triazol-3-yl](methyl)amino]methyl}-1,2,4-oxadiazol-5-yl)benzonitrile

Structure	Example No.	Name	^{1}H-NMR
	988	3-(3-{[methyl(4-methyl-5-pyridin-4-yl-4*H*-1,2,4-triazol-3-yl)amino]methyl}-1,2,4-oxadiazol-5-yl)benzonitrile	8.41(s, 1H), 8.33 (d, 2H), 7.88 (d, 2H), 7.71-7.65 (m, 3H), 4.61 (s, 2H), 3.73 (s, 3H), 3.09 (s, 3H).

	989	3-(3-{[3-(2-methoxypyridin-4-yl)-6,7-dihydro[1,2,4]triazolo[4,3-*a*]pyrimidin-8(5*H*)-yl]methyl}-1,2,4-oxadiazol-5-yl)benzonitrile	8.40 (s, 1H), 8.32 (d, 1H), 8.24 (d, 1H), 7.86 (d, 1H), 7.68 (t, 1H), 7.24 (d, 1H), 6.97 (s, 1H), 5.05 (s, 2H), 4.13 (t, 2H), 3.96 (s, 3H), 3.57 (t, 2H), 2.23 (m, 2H).
	990	N-{1-[5-(3-chlorophenyl)-1,2,4-oxadiazol-3-yl]ethyl}-N,4-dimethyl-5-pyridin-4-yl-4H-1,2,4-triazol-3-amine	8.72 (d, 2 H) 8.09 (s, 1 H) 7.98 (d, 1 H) 7.62 (d, 2 H) 7.54 (d, 1 H) 7.44 (t, 1 H) 4.85 (d, 1 H) 3.70 (s, 3 H) 2.95 (s, 3 H) 1.73 (d, 3 H)

[1368] Example 991

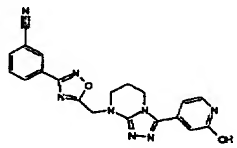
[1369] 3-{5-[(3-pyridin-4-yl-6,7-dihydro[1,2,4]triazolo[4,3-a]pyrimidin-8(5H)-yl)methyl]-1,2,4-oxadiazol-3yl}benzonitrile

[1370] 

[1371] 3-[5-(chloromethyl)-1,2,4-oxadiazol-3-yl]benzonitrile (98.2 mg, 0.447 mmol), and 3-pyridin-4-yl-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyrimidine (62.2 mg, 0.309 mmol) were suspended in acetonitrile (2 ml) and isopropanol (2.4 ml). After stirring for 45 min. potassium carbonate (88.1 mg, 0.637 mmole) was added. The mixture was heated in a microwave oven (130°C) for 30 min. The product was filtered and then purified on prep. HPLC to give 29 mg of the title compound. ^{1}H NMR(DMSO-d6): 8.72 (dd, 2H), 8.36 (br t, 1H), 8.30 (dt, 1H), 8.08 (dt, 1H), 7.79 (t, 1H), 7.68 (dd, 2H), 5.49 (s, 2H), 4.02(t, 2H), 3.3 (m, 1H), 2.36 (s, 3H), 1.71 (t, 2H).

[1372] Example 992

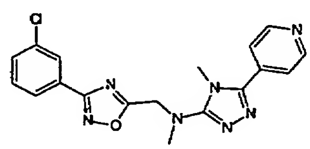
[1373] 3-{5-[3-(2-Hydroxy-pyridin-4-yl)-6,7-dihydro-5H-[1,2,4]triazolo[4,3-a]pyrimidin-8-ylmethyl]-[1,2,4]oxadiazol-3-yl}-benzonitrile

[1374] 

[1375] The title compound was synthesized analogous to 3-{5-[(3-pyridin-4-yl-6,7-dihydro[1,2,4]triazolo[4,3-a]pyrimidin-8(5H)-yl)methyl]-1,2,4-oxadiazol-3yl}benzonitrile. ^{1}H NMR: 8.34 (s, 1 H), 8.29 (d, 1 H), 7.79 (d, 1 H), 7.67 (t, 1 H), 7.38 (d, 1 H), 6.97 (m, 1 H), 6.72 (s, 1 H), 5.13 (s, 2 H), 4.22 (m, 2 H), 3.64 (m, 2 H), 2.27 (m, 2 H).

[1376] Example 993

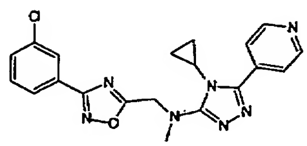
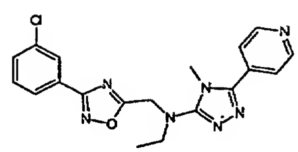
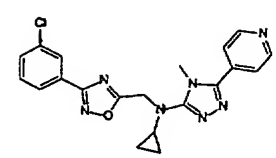
[1377] N-{[3-(3-chlorophenyl)-1,2,4-oxadiazol-5-yl]methyl}-N,4-dimethyl-5-pyridin-4-yl-4H-1,2,4-triazol-3-amine

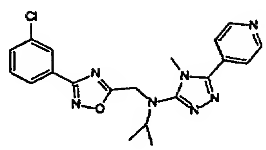
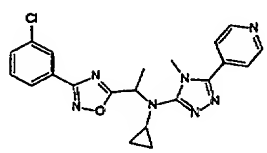
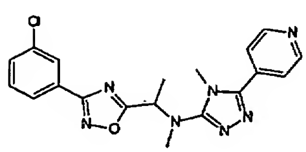
[1378] 

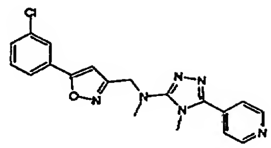
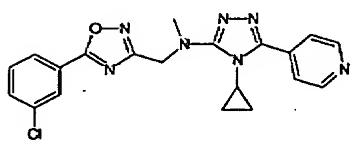
[1379] 1-[3-(3-chloro-phenyl)-[1,2,4]oxadiazol-5-ylmethyl]-1,2,3-trimethyl-isothiourea (55 mg, 0.177 mmol) was mixed with isonicotinic hydrazide (29.1 mg, 0.212 mmol) in ethanol (1 mL) at 85 °C o.n. The reaction mixture was diluted with DCM and washed with water. The product was purified by column chromatography with 5~7 % MeOH in EA and triturated with Et_2O to give the title compound (22.5 mg, 40 %). ^{1}H-NMR: 8.80 (d, 2H), 8.10 (s, 1H), 8.00 (d, 1H), 7.66 (d, 2H), 7.51 (d, 1H), 7.47(t, 1H), 4.80 (s, 2H), 3.74 (s, 3H), 3.15 (s, 3H).

[1380] The following examples were synthesized in a manner analogous to that for N-{[3-(3-chlorophenyl)-1,2,4-oxadiazol-5-yl]methyl}-N,4-dimethyl-5-pyridin-4-yl-

4H-1,2,4-triazol-3-amine

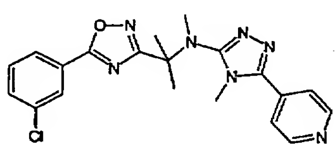
Structure	Example No.	Name	^{1}H-NMR
	994	N-{[3-(3-Chlorophenyl)-1,2,4-oxadiazol-5-yl]methyl}-4-cyclopropyl-N-methyl-5-pyridin-4-yl-4H-1,2,4-triazol-3-amine	8.75(d, 2H), 8.09 (s, 1H), 7.98 (d, 1H), 7.77 (d, 2H), 7.52 (d, 1H), 7.46 (t, 1H), 4.95 (s, 2H), 3.34 (m, 1H), 3.32 (s, 3H) 1.12 (m, 2H) and 0.95 (m, 2H).
	995	[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-ylmethyl]-ethyl-(4-methyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-yl)-amine	8.74 (d, 2H), 8.01 (s, 1H), 7.92 (d, 1H), 7.62 (d, 2H), 7.42 (d, 1H), 7.38 (t, 1H), 4.78 (d, 2H), 3.74 (d, 3H), 3.41 (q, 2H), 1.24 (t, 3H).
	996	[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-ylmethyl]-ethyl-(4-methyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-yl)-amine	8.74 (d, 2H), 8 (s, 1H), 7.89 (d, 1H), 7.62 (d, 2H), 7.44 (d, 1H), 7.41 (t, 1H), 4.87 (s, 2H), 3.76 (s, 3H), 3.12 (m, 1H), 0.82 (br, 2H), 0.7 (br, 2H).

	997	N-{[3-(3-Chlorophenyl)-1,2,4-oxadiazol-5-yl]methyl}-N-isopropyl-4-methyl-5-pyridin-4-yl-4H-1,2,4-triazol-3-amine	8.79 (d, 2H), 8.01 (s, 1H), 8.91 (d, 1H), 7.68 (d, 2H), 7.49 (d, 1H), 7.44 (t, 1H), 4.82 (s, 2H), 3.76 (s, 3H), 3.60 (m, 1H) and 1.35 (d, 6H).
	998	N-{1-[3-(3-Chlorophenyl)-1,2,4-oxadiazol-5-yl]ethyl}-N-cyclopropyl-4-methyl-5-pyridin-4-yl-4H-1,2,4-triazol-3-amine	8.80(d, 2H), 8.09 (s, 1H), 7.99 (d, 1H), 7.68 (d, 2H), 7.52 (d, 1H), 7.47 (t, 1H), 4.92 (q, 1H), 3.71 (s, 3H), 3.07 (m, 1H),1.87 (d, 3H), 0.73 (m, 2H), 0.55 (m, 1H) and 0.42 (m, 1H).
	999	{1-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-ethyl}-methyl-(4-methyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-yl)-amine	8.79 (d, 2H), 8.12 (s, 1H), 8.02 (d, 1H), 7.67 (d, 2H), 7.5 (d, 1H), 7.4 (t, 1H), 5.06 (q, 1H), 3.73 (s, 3H), 3.04 (s, 3H), 1.87 (d, 3H).

	1000	[5-(3-Chloro-phenyl)-isoxazol-3-ylmethyl]-methyl-(4-methyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-yl)-amine	^{1}H NMR ($CDCl_3$) d (ppm): 8.79 (d, 2H), 7.79 (m ,1H), 7.66 (m, 3H), 7.42 (m, 2H), 6.83 (s, 1H), 4.59 (s,2H), 3.69 (s, 3H), 3.00 (s, 3H).
	1001	*N*-{[5-(3-chlorophenyl)-1,2,4-oxadiazol-3-yl]methyl}-4-cyclopropyl-*N*-methyl-5-pyridin-4-yl-4*H*-1,2,4-triazol-3-amine	0.90 (m, 2H) 1.11 (m, 2H) 3.22 (s, 3H) 3.34 (m, 1H) 4.79 (s, 1H) 7.45 (t, 1H) 7.56 (d, 1H) 7.76 (d, 2H) 7.96 (d, 1H) 8.08 (s, 1H) 8.68 (bs, 2H)

[1381] Example 1002

[1382] N-{1-[5-(3-chlorophenyl)-1,2,4-oxadiazol-3-yl]-1-methylethyl}-N,4-dimethyl-5-pyridin-4-yl-4H-1,2,4-triazol-3-amine

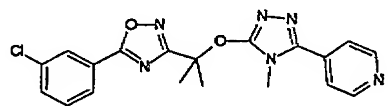
[1383] 

[1384] n-BuLi (132 ml 2.5 M in hex., 0.33 mmol) was added to diisopropyl amine (55 ml, 0.39 mmol). After stirring for 20 minutes at 0°C the mixture was cooled to -78°C and N-{1-[5-(3-chlorophenyl)-1,2,4-oxadiazol-3-yl]ethyl}-N,4-dimethyl-5-pyridin-4-yl-4H-1,2,4-triazol-3-amine (110 mg, 0.28 mmol) was added. After 15 min. methyl iodide (20 µl, 0.33 mmol) was added and the temperature was raised to r.t.

After stirring for 2 h five drops of water were added. After solvent removal *in vacuo*, the crude was taken up in DCM, washed with water and brine, dried and concentrated. The desired product was obtained by prep. HPLC in 20 mg yield. ^{1}H NMR: 1.7 (s, 6 H) 2.8 (s, 3 H) 3.8 (s, 3 H) 7.5 (t, 1 H) 7.6 (d, 1 H) 7.7 (s, 2 H) 8.0 (d, 1 H) 8.1 (s, 1 H) 8.8 (s, 2 H)

[1385] Example 1003

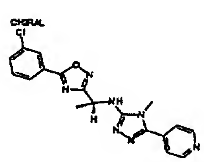
[1386] 4-(5-{1-[5-(3-chlorophenyl)-1,2,4-oxadiazol-3-yl]-1-methylethoxy}-4-methyl-4H-1,2,4-triazol-3-yl)pyridine

[1387] 

[1388] To a solution of diisopropylamine (55.0 ml, 0.39 mmol) in THF (3 ml) at 0°C was added nBuLi (2.5M, hex., 135 ml) slowly. After 20 minutes the mixture was cooled to -78°C and (-)-4-(5-{(1R)-1-[5-(3-chlorophenyl)-1,2,4-oxadiazol-3-yl]ethoxy}-4-methyl-4H-1,2,4-triazol-3-yl)pyridine (107 mg, 0.28 mmol) in THF (2 ml) was added. The resulting mixture was stirred for 45 minutes before CH_3I (22 ml, 0.34 mmol) was added and the reaction mixture was stirred for 1 h at r.t. Sat. NH_4Cl solution was added and the mixture was extracted with EA. The organic phase was washed with H_2O and brine, dried and evaporated. Purification of the residue by silica gel chromatography using $CHCl_3$:MeOH 50:1 followed by prep. HPLC gave the title compound (22 mg, 20%). ^{1}H-NMR: 2.11 (s, 6 H) 3.63 (s, 3 H) 7.45 (d, 1 H) 7.52 - 7.57 (m, 1 H) 7.59 (d, 2 H) 7.98 (d, 1 H) 8.09 (s, 1 H) 8.72 (d, 2 H)

[1389] Example 1004

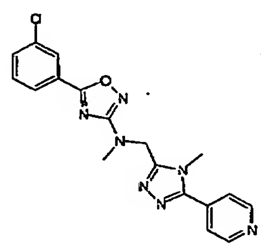
[1390] N-{(1S)-1-[5-(3-chlorophenyl)-1,2,4-oxadiazol-3-yl]ethyl}-4-methyl-5-pyridin-4-yl-4H-1,2,4-triazol-3-amine

[1391] 

[1392] N-{(1S)-1-[5-(3-chlorophenyl)-1,2,4-oxadiazol-3-yl]ethyl}-N,4-dimethyl-5-pyridin-4-yl-4H-1,2,4-triazol-3-amine (3.1 mg, 7.8 mmol) was incubated with human microsome protein (from individual with 70% 3A4) in 50% acetonitrile phosphate buffered at pH 7.4 for 3h and then concentrated under reduced pressure. The mixture was extracted $CHCl_3$. The organic extract was dried and concentrated. Purification by prep. HPLC afforded 0.5 mg (16 %) of the title compound. ^{1}H NMR: 1.77 - 1.83 (d, 3 H) 3.60 (s, 3 H) 5.38 - 5.48 (m, 1 H) 7.48 (m, 1 H) 7.54 - 7.62 (m, 2 H) 8.01 (m, 1 H) 8.12 (m, 1 H) 8.74 (s, 2 H).

[1393] Example 1005

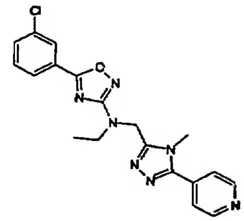
[1394] 5-(3-chlorophenyl)-N-methyl-N-[(4-methyl-5-pyridin-4-yl-4H-1,2,4-triazol-3-yl)methyl]-1,2,4-oxadiazol-3-amine

[1395] 

[1396] NaH (7.0 mg, 0.35 mmol) was added to a solution of 5-(3-chlorophenyl)-N-methyl-1,2,4-oxadiazol-3-amine (60 mg, 0.29 mmol) in DMF (3 ml) at r.t.. After 5 min 4-[5-(chloromethyl)-4-methyl-4H-1,2,4-triazol-3-yl]pyridine (60 mg, 0.29 mmol) dissolved in DMF (3 ml) was added. The reaction mixture was stirred for 4 h at r.t.. Aq. sat. NH_4Cl was added and the mixture was extracted with EA. The organic phase was washed with water and brine, dried and concentrated. Flash chromatography (DCM/MeOH 20:1) afforded 60 mg (54%) of the title compound. ^{1}H NMR: 3.12 (s, 3 H) 3.80 (s, 3 H) 4.94 (s, 2 H) 7.46 (t, 1 H) 7.56 (m, 1 H) 7.58 - 7.63 (m, 2 H) 7.95 (m, 1 H) 8.06 (t, 1 H) 8.79 (m, 2 H).

[1397] Example 1006

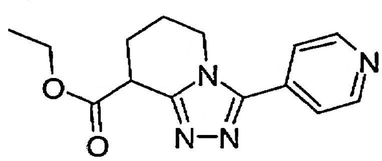
[1398] 5-(3-chlorophenyl)-N-ethyl-N-[(4-methyl-5-pyridin-4-yl-4H-1,2,4-triazol-3-yl)methyl]-1,2,4-oxadiazol-3-amine

[1399] 

[1400] The title compound was prepared analogous to 5-(3-chlorophenyl)-N-methyl-N-[(4-methyl-5-pyridin-4-yl-4H-1,2,4-triazol-3-yl)methyl]-1,2,4-oxadiazol-3-amine. ^{1}H NMR: 1.21 (t, 3 H) 3.53 (q, 2 H) 3.78 (s, 3 H) 4.95 (s, 2 H) 7.46 (d, 1 H) 7.53 (d, 1 H) 7.59 (m, 2 H) 7.95 (m, 1 H) 8.05 (m, 1 H) 8.77 (d, 2 H).

[1401] Example 1007

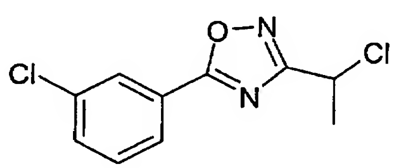
[1402] **Ethyl 3-pyridin-4-yl-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-*a*]pyridine-8-carboxylate**

[1403] 

[1404] The title compound was prepared analogous to 3-pyridin-4-yl-6,7-dihydro-5*H*-pyrrolo[2,1-*c*][1,2,4]triazole from ethyl 2-oxopiperidine-3-carboxylate (2.57 g, 15 mmol), Me_3OBF_4 (2.66 g, 18 mmol) and isonicotinic hydrazide (2.06 g, 15 mmol) in DCM (150 ml) and EtOH (16 ml). Recrystallization from EA afforded 1.67 g (41%). ^{1}H NMR: 1.29 (t, 3 H), 2.03 (m, 1 H), 2.14 - 2.25 (m, 2 H), 2.32 (m, 1 H), 4.01 - 4.12 (m, 1 H), 4.16 - 4.27 (m, 4 H), 7.64 (d, 2 H), 8.74 (d, 2 H)

[1405] Example 1008

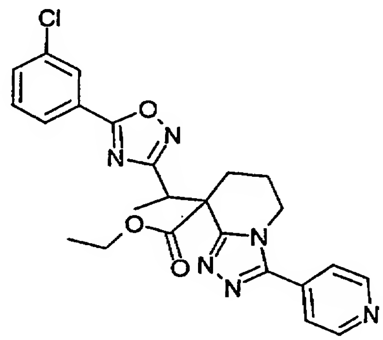
[1406] 3-(1-chloroethyl)-5-(3-chlorophenyl)-1,2,4-oxadiazole

[1407] 

[1408] 5 drops of DMF was added to 1-[5-(3-chlorophenyl)-1,2,4-oxadiazol-3-yl]ethanol (12.3 g, 54.9 mmol) in $SOCl_2$ (150 mL) and the reaction was heated at 70 °C for 5 h. The excess $SOCl_2$ was evaporated and the residue was purified by column chromatography (Hep to Hep-EA 5:1) to give 12.4 g (93 %) of the title compound. ^1H NMR: 1.96 (d, 3H) 5.20 (q, 1H) 7.46 (t, 1H) 7.59 (m, 1H) 8.04 (m, 1H) 8.17 (t, 1H)

[1409] Example 1009

[1410] Ethyl 8-{1-[5-(3-chlorophenyl)-1,2,4-oxadiazol-3-yl]ethyl}-3-pyridin-4-yl-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridine-8-carboxylate



[1411]

[1412] A solution of ethyl 3-pyridin-4-yl-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-*a*]pyridine-8-carboxylate (182 mg, 0.67 mmol) in DMF (2 ml) was added to a stirred mixture of NaH (20 mg, 0.81 mmol) in DMF (2 ml). After 45 min a solution of 3-(1-chloroethyl)-5-(3-chlorophenyl)-1,2,4-oxadiazole (180 mg, 0.74 mmol) in DMF (1 ml) was added and the resulting solution was stirred at 65 °C for 3 h and then cooled to r.t. Aq. sat. NH_4Cl solution was added and the mixture was extracted with EA. The organic phase was washed with water and brine, dried and concentrated. Column chromatography (DCM/MeOH 20:1) gave 207 mg (65%) of the title compound as a diastereomeric mixture. ^1H NMR: 1.27 (t, 3 H), 1.34 (t, 3 H), 1.48 (d, 3 H), 1.55 (d, 3 H), 2.15 (m, 2 H), 2. 18 (m, 4 H), 2.61 (m, 2 H), 4.00 (m, 2 H), 4.18 - 4.29 (m, 4 H), 4.30 - 4.40 (m, 2 H), 4.55 (q, 1 H), 4.65 (q, 1 H), 7.37 (t, 1 H), 7.44 (t, 1 H), 7.50 (m, 1 H), 7.55 (m, 1 H), 7.63 (d, 2 H), 7.69 (d, 2 H), 7.83 (m, 1 H), 7.92 (m, 1 H), 7.95 (m, 1 H), 8.05 (m, 1 H), 8.75 (d, 2H), 8.76 (d, 2 H)

[1413] Pharmaceutical Examples

[1414] FLIPR Assay of Group I receptor antagonist activity

[1415] For FLIPR analysis, cells were seeded on collagen coated clear bottom 96-well plates with black sides and analysis of $[Ca^{2+}]_i$ mobilization was performed 24 hours following seeding. Cell cultures in the 96-well plates were loaded with a 4 μM solution of acetoxymethyl ester form of the fluorescent calcium indicator fluor-3 (Molecular Probes, Eugene, Oregon) in 0.01% pluronic. All assays were performed in a buffer containing 127 mM NaCl, 5 mM KCl, 2 mM $MgCl_2$, 0.7 mM NaH_2PO_4, 2 mM $CaCl_2$, 0.422 mg/ml $NaHCO_3$, 2.4 mg/ml HEPES, 1.8 mg/ml glucose and 1 mg/ml BSA Fraction IV (pH 7.4).

[1416] FLIPR experiments were done using a laser setting of 0.800 W and a 0.4 second CCD camera shutter speed with excitation and emission wavelengths of 488 nm and 562 nm, respectively. Each FLIPR experiment was initiated with 160 μL of buffer present in each well of the cell plate. A 40 μL addition from the antagonist plate was followed by a 50 μL addition from the agonist plate. After each addition the fluorescence signal was sampled 50 times at 1 second intervals followed by 3 samples at 5 second intervals. Responses were measured as the peak height of the response within the sample period.

[1417] EC_{50}/IC_{50} determinations were made from data obtained from 8 point concentration response curves (CRC) performed in duplicate. Agonist CRC were generated by scaling all responses to the maximal response observed for the plate. Antagonist block of the agonist challenge was normalized to the average response of the agonist challenge in 14 control wells on the same plate.

[1418] Measurement of Inositol Phosphate (IP3) Turnover in Intact Whole Cells

[1419] GHEK stably expressing the human mGluR5d receptor were seeded onto 24 well poly-L-lysine coated plates at 40 x 10^4 cells /well in media containing 1 μCi/well [3H] myo-inositol. Cells were incubated overnight (16 h), then washed three times and incubated for 1 hour at 37°C in HEPES buffered saline (146 mM NaCl, 4.2 mM KCl, 0.5 mM $MgCl_2$, 0.1% glucose, 20 mM HEPES, pH 7.4) supplemented with 1

unit/ml glutamate pyruvate transaminase and 2 mM pyruvate. Cells were washed once in HEPES buffered saline and pre-incubated for 10 minutes in HEPES buffered saline containing 10 mM LiCl. Compounds (agonists) were added and incubated at 37°C for 30 minutes. Antagonist activity was determined by pre-incubating test compounds for 15 minutes, then incubating in the presence of glutamate (80μM) or DHPG (30 μM) for 30 minutes. The reaction was terminated by the addition of 0.5 ml perchloric acid (5%) on ice, with incubation at 4°C for at least 30 minutes. Samples were collected in 15 ml Falcon tubes and inositol phosphates were separated using Dowex columns, as described below.

[1420] Assay For Inositol Phosphates Using Gravity-Fed Ion-Exchange Columns

[1421] Preparation of Ion- Exchange Columns

[1422] Ion-exchange resin (Dowex AG1-X8 formate form, 200-400 mesh, BIORAD) was washed three times with distilled water and stored at 4°C. 1.6 ml resin was added to each column and washed with 3 ml 2.5 mM HEPES, 0.5 mM EDTA, pH 7.4.

[1423] Sample Treatment

[1424] Samples were collected in 15 ml Falcon tubes and neutralized with 0.375 M HEPES, 0.75 M KOH. 4 ml of HEPES / EDTA (2.5 / 0.5 mM, pH 7.4) were added to precipitate the potassium perchlorate. Supernatant was added to the prepared Dowex columns.

[1425] Inositol Phosphate Separation

[1426] Elute glycero phosphatidyl inositols with 8 ml 30 mM ammonium formate.

[1427] Elute total inositol phosphates with 8 ml 700 mM ammonium formate / 100 mM formic acid and collect eluate in scintillation vials. Count eluate mixed with 8 ml scintillant.

[1428] Screening for compounds active against tlesr

[1429] Adult Labrador retrievers of both genders, trained to stand in a Pavlov sling, are used. Mucosa-to-skin esophagostomies are formed and the dogs are allowed to recover completely before any experiments are done.

[1430] Motility measurement

[1431] In brief, after fasting for approximately 17 h with free supply of water, a multilumen sleeve/sidehole assembly (Dentsleeve, Adelaide, South Australia) is introduced through the esophagostomy to measure gastric, lower esophageal sphincter (LES) and esophageal pressures. The assembly is perfused with water using a low-compliance manometric perfusion pump (Dentsleeve, Adelaide, South Australia). An air-perfused tube is passed in the oral direction to measure swallows, and an antimony electrode monitored pH, 3 cm above the LES. All signals are amplified and acquired on a personal computer at 10 Hz.

[1432] When a baseline measurement free from fasting gastric/LES phase III motor activity has been obtained, placebo (0.9% NaCl) or test compound is administered intravenously (i.v., 0.5 ml/kg) in a foreleg vein. Ten min after i.v. administration, a nutrient meal (10% peptone, 5% D-glucose, 5% Intralipid, pH 3.0) is infused into the stomach through the central lumen of the assembly at 100 ml/min to a final volume of 30 ml/kg. The infusion of the nutrient meal is followed by air infusion at a rate of 500 ml/min until an intragastric pressure of 10±1 mmHg is obtained. The pressure is then maintained at this level throughout the experiment using the infusion pump for further air infusion or for venting air from the stomach. The experimental time from start of nutrient infusion to end of air insufflation is 45 min. The procedure has been validated as a reliable means of triggering TLESRs.

[1433] TLESRs is defined as a decrease in lower esophageal sphincter pressure (with reference to intragastric pressure) at a rate of >1 mmHg/s. The relaxation should not be preceded by a pharyngeal signal ≤2s before its onset in which case the relaxation is classified as swallow-induced. The pressure difference between the LES and the stomach should be less than 2 mmHg, and the duration of the complete relaxation longer than 1 s.

[1434] Abbreviations

BSA	Bovine Serum Albumin
CCD	Charge Coupled Device
CRC	Concentration Response Curve
DHPG	3,5-dihydroxyphenylglycine;
EDTA	Ethylene Diamine Tetraacetic Acid
FLIPR	Fluorometric Imaging Plate reader
GHEK	GLAST-containing Human Embrionic Kidney
GLAST	glutamate/aspartate transporter
HEPES	4-(2-hydroxyethyl)-1-piperazineethanesulfonic acid (buffer)
IP_3	inositol triphosphate

[1435] Results

[1436] Typical IC_{50} values as measured in the assays described above are 10 μM or less. In one aspect of the invention the IC_{50} is below 2 μM. In another aspect of the invention the IC_{50} is below 0.2 μM. In a further aspect of the invention the IC_{50} is below 0.05 μM.